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ON THE PATHOGENESIS OF THE SIGNS OF TRAUBE AND DUROZIEZ IN AORTIC INSUFFICIENCY. A GRAPHIC STUDY

ALDO A. LUISADA, M.D.
BOSTON, MASS.

PROPER evaluation of acoustic phenomena in peripheral arteries is very important for the understanding of the hemodynamics of aortic regurgitation. Therefore, a series of observations based upon exact graphic records, and not on subjective appreciation, will be of some interest.

The acoustic phenomena in peripheral arteries in aortic insufficiency were studied a long time ago, mostly on the femoral artery.

In 1841, Bouillaud[2] described a double *murmur* in the femoral arteries of patients with this valvular disease. In 1861, his pupil Duroziez[4] emphasized the significance of this double murmur (double souffle). He studied the conditions of its appearance (marked compression with the stethoscope) and emphasized it so that it was accepted as a typical sign of aortic regurgitation.

A few years later, Traube[22, 6] described a double *tone* (Doppelton) which can be heard in rare cases by applying the stethoscope lightly on the femoral artery, so that the diameter of the vessel is not modified by the compression.

The fundamental work of Duroziez and Traube made many points clear concerning the causation of these murmurs and sounds.

1. The double tone is a rare phenomenon, the double murmur is frequent (Traube).

2. The double tone is a spontaneous phenomenon in the arterial wall (Traube). The double murmur, on the contrary, is an artificial phenomenon caused by eddies in the blood stream produced by compression with the stethoscope (Duroziez, Traube).

3. If the stethoscope is lightly applied on the artery, it is also possible to produce the first murmur by compressing the vessel *above* the stethoscope. The appearance of the second murmur, on the contrary, is favored more by compressing the vessel below it (Traube[22]).

4. Neither phenomenon is typical of aortic regurgitation. The double

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tone can be observed during fever (Fräntzel,[6] Traube[22]), and the double murmur in typhoid fever, chlorosis, and saturnism (Duroziez[4]).

These observations afford a clear distinction between the two vascular phenomena, in spite of the confusion introduced by later workers.

The first arterial murmur was explained as caused by the eddies which are formed by the pulse wave under the narrow arterial section where the stethoscope is applied.

The first of the two sounds described by Traube seemed to be caused by the quick distension of the artery, because of the typical character of the pulse (pistol-shot sound). On the contrary, the second sound and the second murmur were differently explained, and numerous investigations were made in order to ascertain their meaning.

The second *tone* described by Traube was explained by him as caused by the rapid change of tension of the arterial wall after the quick distension.

The second *murmur* was explained by Duroziez as caused by a backward wave coming from the periphery. His own words were: ". . . le sang de tout l'arbre artériel, arreté par la contraction des artérioles, récule et, rencontrant à son tour un retrécissement, il souffle comme il a soufflé en avant. . . . Les deux souffles vont en sens contraire; c'est un mouvement de va-et-viens."

A few years later Toussaint and Colrat[21] advanced the hypothesis that the second murmur was caused by the dicrotic wave. Therefore, they admitted a double centrifugal movement of the blood stream under the stethoscope (double souffle en avant). The *centripetal nature* of the wave causing the second murmur was, however, admitted by all later authors. Since a total reflux from the periphery could not be easily visualized, the old theory was replaced by that of a local reflux. This would be caused by the marked difference in pressure in the two arterial sections which are separated by the stethoscope. This new concept was first advanced by Potain,[17] then discussed and accepted by Ferrio and Bosio,[5] and was further amplified by Gallavardin.[7]

The double femoral murmur is found in certain patients who do not have aortic regurgitation. Its occurrence in patients with conditions which accelerate the circulation was first observed by Duroziez.

Ferrio and Bosio,[5] Tice,[20] Laubry and his co-workers,[9] and Blumgart and Ernstene[3] studied it in patients without aortic insufficiency.

The studies of Ferrio, Laubry, and Blumgart need further discussion, because their observations are partly contradictory. Ferrio and Bosio[5] found that the application of an elastic band to the leg may cause the appearance of a double murmur in the femoral arteries of normal people. The same device increases the double murmur of patients with aortic insufficiency.

Laubry, Brosse, and van Bogaert[9] found that a peripheral obstacle, namely, a pneumatic cuff inflated nearly to the level of the systolic pressure, increases the intensity of the second murmur in aortic insufficiency. In arterial hypertension, compression below the stethoscope causes the

appearance either of a diastolic sound or a diastolic murmur. They confirm, therefore, the old observations of Traube. Quite different were the observations of Blumgart and Ernstene[3] in their study of the double murmur in both the femoral and brachial artery. They found that applying a pneumatic cuff to the forearm and inflating it below the diastolic pressure abolished the second murmur in patients without aortic insufficiency (thyrotoxicosis, hypertension, normals). On the contrary, pressure with the upper edge of the stethoscope bell increased the murmur in the same patients. In patients with aortic insufficiency the second murmur was increased by the same pneumatic device and by compression with the lower edge of the stethoscope bell. In accordance with their own observations, Ferrio and Bosio, as well as Laubry, Brosse, and van Bogaert, believe that the second murmur is caused by backward flow in patients both with and without aortic regurgitation. Blumgart and Ernstene, on the contrary, admit a double mechanism: backward flow when there is aortic insufficiency, and forward flow when this condition is absent.

Summarizing the preceding studies, an increase in the intensity of the second murmur (and also of the second tone) was produced by applying a distal obstacle to the arterial flow in patients with aortic insufficiency. Contradictory results are reported on patients without aortic insufficiency; Blumgart and Ernstene observed disappearance of the murmur with a distal obstacle, but all others observed an increase (Traube; Ferrio and Bosio; Laubry, Brosse, and van Bogaert). As the former inflated the cuff below diastolic pressure, the latter much above it, the difference might be the result of using a different technique.

Further observations were made by Laubry and his co-workers[9] concerning another murmur which may be caused by the second top of the pulse wave when there is anacrotism. In such cases there is a double murmur at first (main wave with anacrotic depression), and another murmur later (equivalent to the second murmur of Duroziez).

A few years earlier, a graphic study of the double murmur was made by Pasoli.[16] In spite of a still incompletely developed phonocardiographic technique, he was able to record the first and second murmur. Among the chief results of his study were: (1) demonstration that there is no abnormal deformity of the pulse curve during the second murmur; (2) proof that, at the time of the second murmur, the pulse in the dorsalis pedis artery is still near the top. Pasoli admitted that the second murmur was caused by a second forward movement of the blood stream, produced by a local contraction of the artery.

TECHNIQUE

The acoustic vibrations of the arteries were recorded by means of a Stetho-Cardiette (Sanborn). This apparatus made possible a simultaneous recording of other tracings.

The first experiments were done with the original technique of Traube and Duroziez, but by substituting for the stethoscope, a microphone with an open funnel. Comparison was made between records with a stetho-

scopic microphone and those with a logarithmic microphone; the latter is more similar to the human ear. The audiophone enabled one to hear the sounds and murmurs during the taking of the records. A further study was made with microphones closed by a membrane which gives better tracings of high-pitched murmurs (Rappaport and Sprague[18]).

After ascertaining the type of murmurs and sounds which are typical of the femoral artery, attempts were made to obtain simultaneous recordings of sounds and arterial pulse at the seat of application of the stethoscope. This was done by using the special funnel and the crystal microphone described by Miller and White[15] for venous pulse records.

Since it is very important to follow the pulse wave in its peripheral course after it has passed under the stethoscope, records were made in which the femoral sounds were recorded simultaneously with either a low tibial pulse or a foot pulse. The former was recorded by means of a pneumatic cuff and a new apparatus recently studied by Rappaport and Luisada.[12] A further problem, that of recording at the same time the femoral sounds and the heart sounds, was solved in the following way: Two absolutely identical Stetho-Cardiettes were used. One recorded Lead I of the electrocardiogram and the heart sounds over the aortic area. The other recorded Lead I of the electrocardiogram and the femoral sounds. The tracings were taken simultaneously at a film speed of 75 mm. per second. Both motors were started at the same time and simultaneous signals were written from time to time on both records. The signals made possible a comparison of the records. The ventricular complex of the electrocardiogram made possible an absolutely exact superimposition.

A similar technique was used for recording the arterial sounds either above and below a compression, or at different points of the femoral artery. A pneumatic cuff was applied on the limb. Two microphones were applied on the artery, above and below the cuff (Fig. 1*B*). In other experiments the cuff was displaced downwards, either just above or just below the knee. Two microphones were applied on the thigh. The upper compressed the femoral at the groin and produced the double murmur, and the lower was applied with just slight compression on the thigh. A test was made to ascertain that the latter was not producing any local murmur before starting the compression with the upper microphone (Fig. 1*A*).

The same technique was later used for the arm. Two Stetho-Cardiettes recorded the two phonoarteriograms simultaneously. Electrocardiograms and signals were recorded as mentioned above.

Later, two microphones were applied either 5 or 10 inches apart on the femoral artery. Two pneumatic cuffs gave the same light pressure to them. A test was made in order to exclude any local production of murmurs. Then another cuff was inflated to a high pressure below the lower microphone.

In a further series of experiments the changes induced by compression either above or below the seat of appearance of a murmur were investigated. For this purpose I used the apparatus described by Rappaport and myself[12] for blood pressure records. This contains a double microphone and is connected to a double pneumatic cuff. The upper cuff is inflated to a known pressure, and the lower cuff is connected to both microphones, giving two tracings, i.e., that of the pulse and that of the sounds. The device was employed in the routine way for the study of sounds and pulse below the compression. The order in which

the cuffs were applied was later reversed in order to study sounds and pulse above the compression (Fig. 1*C*).

This work was performed on twenty-two patients from different hospitals.* Eight of them had syphilitic aortic insufficiency, nine had rheumatic aortic insufficiency, and five had arteriosclerotic aortic insufficiency. Seven additional patients had arterial hypertension, and four subjects were normal students into whom different drugs were injected.

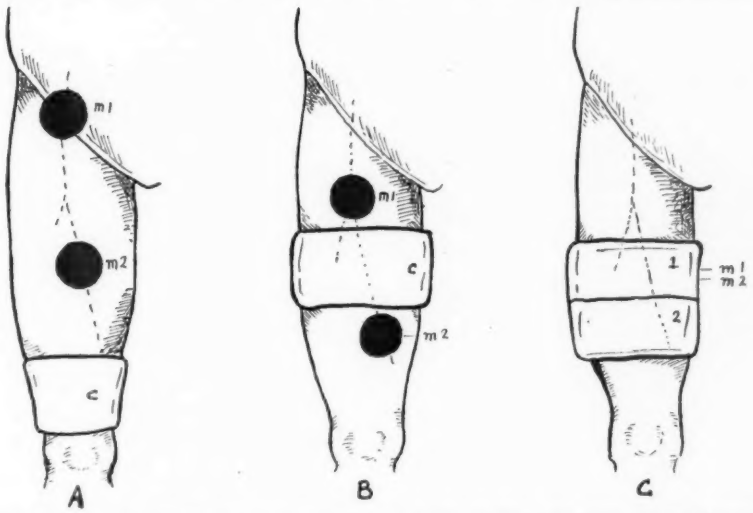

Fig. 1.—Different techniques for recording the femoral sounds above and below compression. *m1, m2,* microphones; *c,* cuff.

RESULTS

1. Aspects and Phase of the First Murmur.—The first murmur upon compression of the arteries is a constant feature which can be observed on normal people as well as on patients with aortic regurgitation. It starts slightly before the rise of the volume curve of the pulse and lasts during the ascending phase and slightly after the top. The first fact is due to eddies formed during the cessation of collapse of the artery which is closed by the compression (Fig. 2*A*).

The aspect of this murmur changes, depending upon the kind of microphone employed. It starts with a sudden multiple vibration, representing a snap, just before the dilatation of the artery. This is best recorded by a stethoscopic microphone. Then many multiple and high-pitched vibrations occur, which are best recorded by a logarithmic microphone (Fig. 2*B* and *C*). When the pulse wave has either a rounded ascending phase or an anacrotic depression, the first murmur lasts until the second top and slightly beyond it. In such cases a double murmur in the first phase is not unusual. When, on the contrary, the pulse wave rises abruptly and is followed by a rapid descent, the murmur lasts well beyond

*The Beth Israel Hospital, the Boston City Hospital, and the Medfield State Hospital. I wish to express my gratitude to Dr. H. L. Blumgart and Dr. M. D. Altschule, as well as to Dr. L. B. Ellis and Dr. Axelson, for granting me the opportunity to study the patients.

the top. The average length of this murmur is 0.12 second. The maximal length was 0.20 second.

Records taken with the microphone of the blood pressure recording set showed a series of vibrations of a lower frequency, representing a very rough murmur. In general, the brachial shows a rougher murmur and slower vibrations than the femoral artery (Fig. 4).

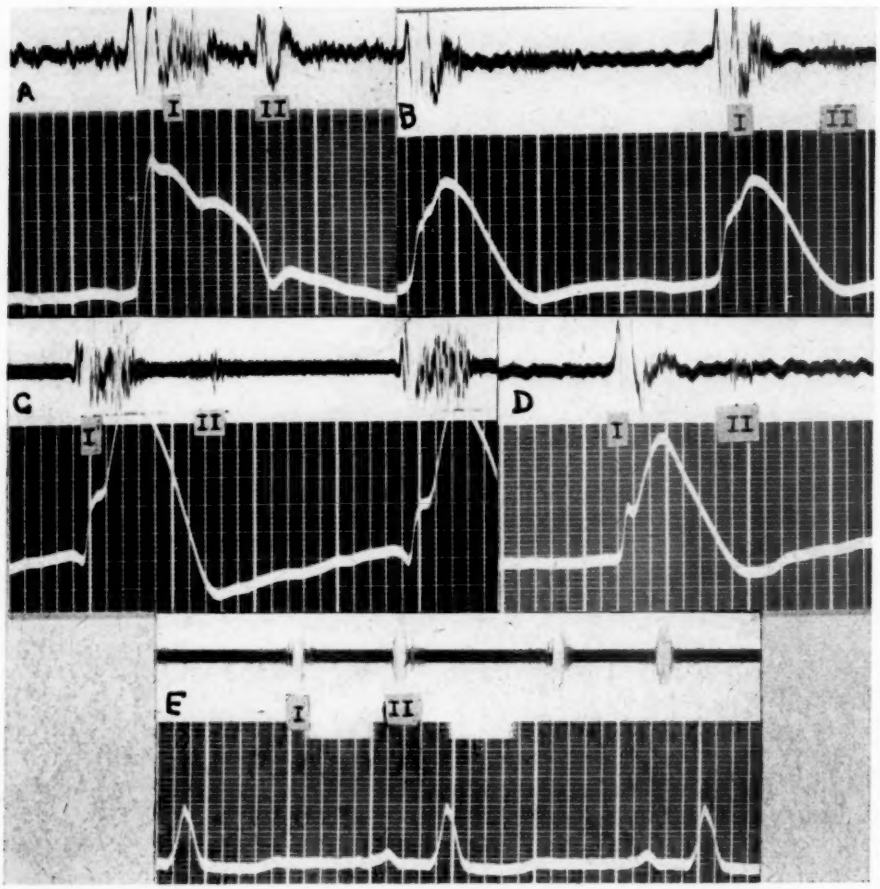

Fig. 2.—Femoral sounds and femoral pulse at the groin in different patients. The pulse is recorded at the site of compression. *A*, usual (stethoscopic) microphone; *B*, *C*, *D*, and *E*, special (logarithmic) microphone. *A*, Mitral and aortic regurgitation; *B*, syphilitic aortic regurgitation; *C*, double aortic defect; *D*, normal student after injection of 1 mg. of adrenalin; *E*, electrocardiogram and femoral sounds in a case of syphilitic aortic regurgitation. The femoral sounds were recorded by means of a logarithmic microphone, applied lightly above a cuff compressing the lower part of the thigh.

2. Aspects of the Second Murmur.—The aspect of the second murmur depends upon the microphone used. A stethoscopic microphone often shows a large and slow deflection, on which more frequent vibrations are superimposed (Fig. 2*A*). Marked individual variations were found. The murmur may be very short, consisting of only 5 to 6 quick vibrations,

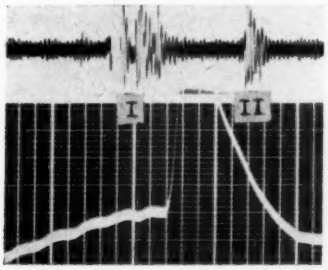

Fig. 3.—Femoral sounds at the groin and dorsalis pedis pulse in two cases of double aortic defect.

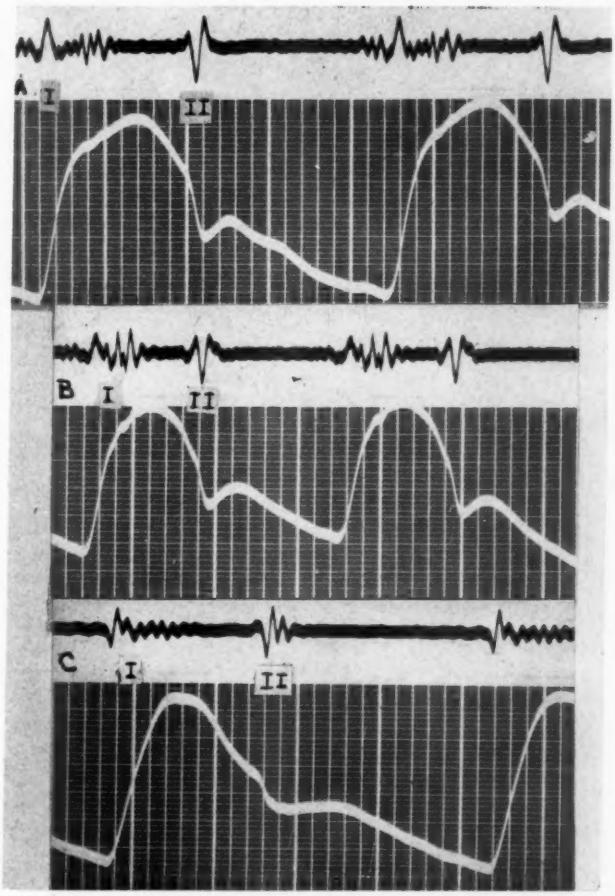

Fig. 4.—Brachial sounds and pulse recorded by means of the blood pressure recording set (like Fig. 1*C*, but inverted). *A*, Syphilitic aortic regurgitation (blood pressure 160/50; recording cuff, 30; compression, 140). *B*, Hypertension, no aortic regurgitation (blood pressure 165/80; recording cuff, 40; compression, 145). *C*, Normal student (after adrenalin, blood pressure, 140/60; recording cuff, 40; compression, 120). In all three the second murmur is represented in the records by a snap. At the femoral there was a double murmur.

and lasting 0.06 second. It may be much longer, lasting even 0.14 second. The murmur is usually shorter in the brachial and longer in the femoral artery. It may be represented only by a single or double vibration. In that case we should call it a snap, or a tone, not a real murmur. Tones are more frequently found in the brachial than in the femoral artery (Fig. 4).

3. Phase of the Second Murmur.—The second murmur in the femoral artery occurs some time after the second heart sound. In one case in which an exact measurement was made, a delay of 0.12 second from the beginning of the second aortic sound was found. In this case the second arterial murmur occurred when the maximal amplitude of the aortic diastolic murmur had already subsided. The comparative study was suggested by the desire to ascertain the exact relationship between second femoral murmur and phase of regurgitation, as evidenced by the diastolic murmur over the aortic area.

The second murmur in the arteries has a definite relationship to the shape and phase of the arterial pulse at the point of observation. When no appreciable dicrotic wave was present in our records, and the pulse showed only an ascending and a descending phase, the second murmur occurred at the time of the lowest point of the descending phase. When a clearly defined dicrotic wave was present, the second murmur occurred at the bottom of the depression preceding the dicrotic wave. This occurred constantly, in the brachial as well as the femoral artery. When, instead of the murmur, there was a snap or tone, this also coincided with the depression preceding the dicrotic wave (Fig. 4). Sometimes, however, this coincided with the descending phase of the main wave. When the murmur or tone was present in patients without aortic regurgitation, the same time relationship and the same connection with the phase of the pulse was found. When the murmur was a prolonged one, it lasted during part of the ascending phase of the dicrotic wave.

Simultaneous registration of the sounds in the femoral artery and the pulse curve in the dorsalis pedis artery of the same side showed that the second murmur falls during the descending phase of that peripheral pulse, and sometimes is very near the peak of the pulse wave in that distant artery (Fig. 3).

A careful study which was made in order to ascertain whether any abnormal depression of the pulse curve coincided with the second murmur failed to reveal any.* This murmur is always present during the predicrotic depression. In one record, taken on the brachial artery, on the contrary, a small additional wave was found in the pulse curve at the time of the second murmur and during the predicrotic depression. This could be attributed, however, to an artifact.

4. Pressure Necessary to Cause the Second Murmur.—It is apparent that no exact evaluation of the compression is possible when this is

*Since the second murmur was attributed to abnormal pressure conditions caused by the stethoscope, theoretically it would be possible to observe an abnormal deformity of the pulse curve.

effected directly, either by the stethoscope or by the microphone. On the contrary, it was possible to ascertain it by the following device. A double pneumatic cuff was applied to the thigh, the lower part of which exerted a known pressure. The upper part recorded pulse wave and arterial murmurs under a very low inflation pressure (20 mm. Hg). This device was also found best for recording the double murmur (see later).

Studying the records at gradually increasing pressures shows that the second murmur starts approximately at a compression midway between systolic and diastolic pressure. The second murmur increases in loudness until the compression is 25 per cent lower than the systolic, and then decreases again. Complete obliteration of the peripheral tract of the artery causes disappearance of the murmur. The optimum compression seems to be, therefore, about three-fourths of the way up from the diastolic to the systolic. For instance, in patients with a pressure of 200/60, the murmur starts around 130, increases up to 165, and becomes fainter above that figure.

In most of the cases, the compression causing the murmur was also the best for obtaining a good pulse tracing in all its details. As is known, a good pulse curve is obtained with the oscillographs when the artery is compressed above the average arithmetic pressure and below the systolic. As confirmation of this, patients with a good dicrotic wave showed the maximum height of this wave with the amount of compression which gave the best intensity of the second murmur. This was true for the brachial, as well as for the femoral artery, and was also true in patients who had the second murmur, but no aortic regurgitation.

5. Conditions Favoring the Appearance of the Second Murmur.—Comparison of the stethoscopic records taken *above* and those taken *below* the compression of a pneumatic cuff shows how the obstacle may influence the murmur. In patients with aortic regurgitation the murmur was always clearer and better in the microphone above, than in that below, the compression (Fig. 5). It was not unusual to see and hear a double murmur above, and a simple sound (equivalent to the first murmur) below, the compression. Patients without aortic regurgitation showed exactly the same behavior.

A rapid peripheral circulation and a high pulse pressure were the conditions under which the second murmur was found, even without aortic regurgitation. The pulse curve above the compression showed an increased dicrotic wave, and that below the compression showed none. Records taken above a compression, but at different distances from it, showed that the murmur starts about 10 inches above a compression cuff, but becomes louder and louder until the immediate vicinity of the cuff is reached.

6. Transmission of the Murmur and Direction of the Blood Flow Causing It.—In all records taken on the femoral artery by means of

two microphones, the first murmur was recorded slightly later with the second microphone than with the first. The delay of 0.02 to 0.04 second was simply the time necessary for the pulse wave to reach the second microphone.

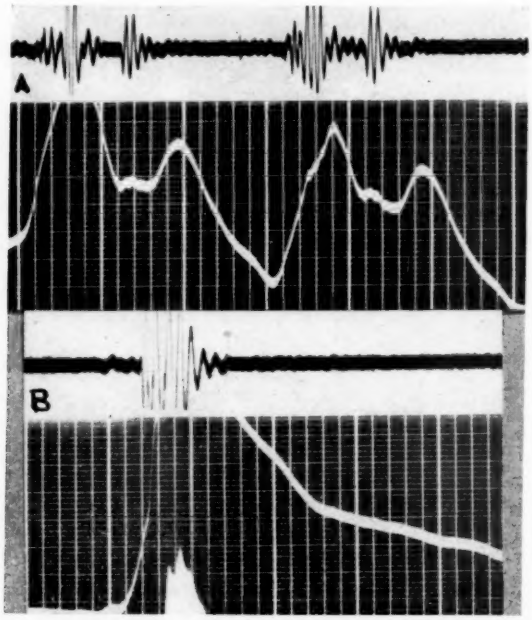

Fig. 5.—Double murmur recorded at the thigh by means of the blood pressure recording set (like Fig. 1*C*, but inverted). *A*, Records above the compression; *B*, records below the compression; (blood pressure, thigh, 250/80; recording cuff, 20; compression, 180).

In practically all femoral records the second murmur also occurs later on the second microphone (Fig. 6). The delay between appearance on the first and second microphones varies from 0.02 to 0.04 second. The different distance between the two microphones and the different speed of the pulse wave in different patients explain the different results obtained. The delay between the two second murmurs is sometimes equal to that between the two first murmurs, but is usually slightly longer. The records taken on the arm did not give such definite results; in most of them both murmurs were simultaneous. Only in a few of them was a minimal delay present, and then in the same sense as in the thigh. However, even in the arm, no precession of the second murmur was ever recorded in the upper microphone.

DISCUSSION

Our study gives exact data about the second murmur of Duroziez's sign. This murmur is actually linked to a definite phase of the pulse wave, for it occurs between the main wave and the dicrotic wave. Conditions for its occurrence are, first, a high pulse pressure, and, second, a high dicrotic wave. Every condition which increases the previous two

will either cause the appearance, or increase the intensity, of the second murmur. Compression of the artery at a level between average pressure and systolic pressure increases the height of the dicrotic wave at the seat of compression and above it, and decreases the dicrotic wave below it. The same compression causes appearance of the second murmur at the seat of compression and above it, but does not cause any murmur below it.

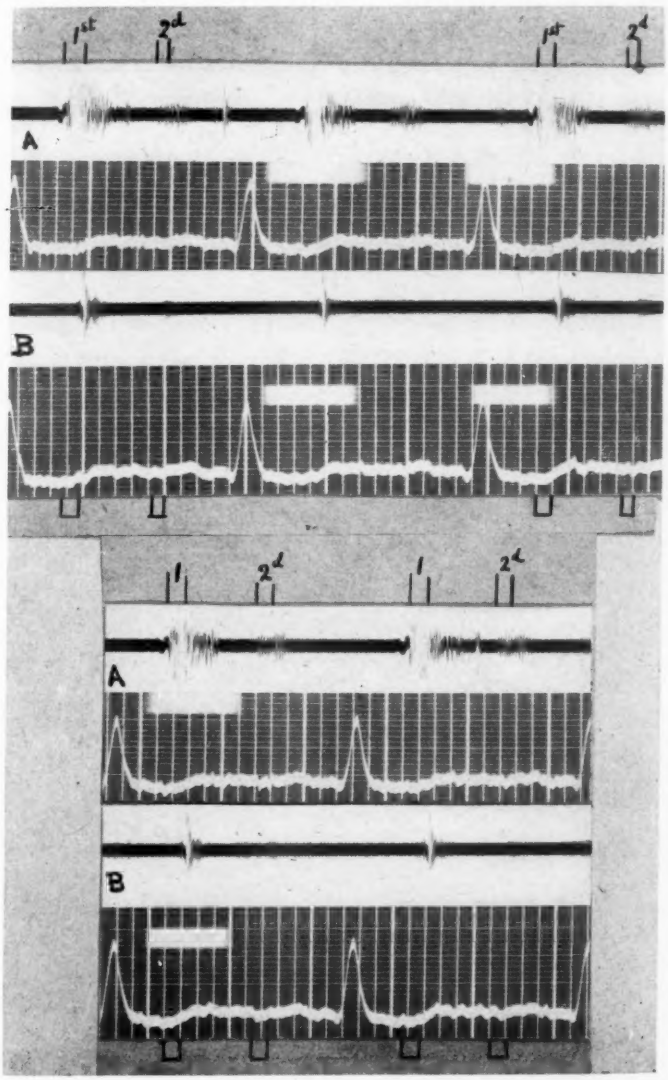

Fig. 6.—Delay between the first and second murmur, shown by placing two microphones 10 inches apart. *A*, Upper microphone over the groin (compression); *B*, lower microphone lightly applied over the thigh; a compression cuff is applied below the knee. The lower microphone does not record any murmur when no compression is applied on the upper microphone (Fig. 1*A*).

This is true in patients both with and without aortic regurgitation. Drugs which stimulate the circulation and increase the pulse pressure may cause the appearance of the second murmur in normal persons. There is a general unity of view in admitting that both murmurs of Duroziez's sign are caused by eddies in the blood stream. Since "fluid" murmurs radiate in the direction of the blood stream which causes them, the time of appearance of the murmur at different points along the femoral artery should give a clue about direction of the blood flow during the murmur. As a matter of fact, our records show that the second murmur occurs slightly later in a more peripheral part of the artery than in a more central. This is evidence that the blood flow is centrifugal at the time of the murmur.

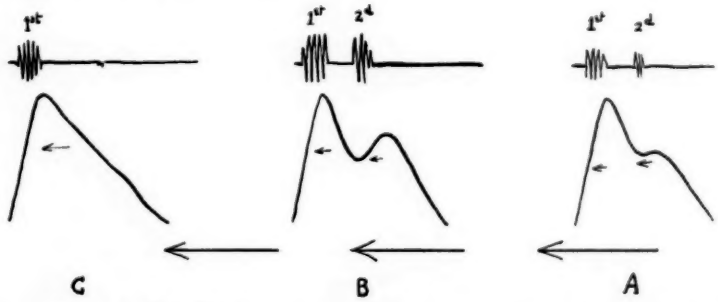

Fig. 7.—Sketch of the changes of the pulse curve and of the arterial sounds in passing under a compression. *A*, Above the compression; *B*, at the seat of compression; *C*, below the compression. The direction of the blood flow is from right to left.

The delay between the vibrations of the second murmur when it is recorded at different points along the same artery is often slightly longer than that between the vibrations of the first murmur. This fact points to a slower speed of the stream during the second murmur, in contrast with that during the first.

A definite explanation of the phenomenon cannot avoid taking into account the nature of the dicrotic wave. When ventricular systole ends, and pressure eddies cause closure of the aortic valve, a rebound of the aortic wall forces the blood centrally as well as toward the periphery. In aortic insufficiency this rebound is much greater, and enables the pulse wave to follow its peripheral course in spite of regurgitation of blood which probably affects directly only the initial part of the arterial tree.

Under normal conditions the swing of the blood column towards the heart sets up a negative wave which travels toward the periphery behind the main wave, and is represented by the predicrotic notch of the pulse curve. In patients with aortic regurgitation there is no reason for admitting any other mechanism. In spite of the valvular incompetence, the aortic valves still represent an obstacle, and this is increased by the muscular tonus of the infundibular part of the left ventricle. Records taken on different arteries of patients with aortic regurgitation show

that the predicrotic notch occurs later in peripheral than in central arteries. This shows that the negative wave has a centrifugal course. After closure of the aortic valves the blood column rebounds abruptly from their surface and sets up a second positive wave which will follow the predicrotic notch toward the periphery. Here, also, there is no fundamental difference between patients with aortic insufficiency and others. The initial phenomena are further influenced by the action of the peripheral arteries, which deepens the predicrotic notch and rounds out the dicrotic wave.

The speed of both the predicrotic notch and the dicrotic wave is slightly less than that of the main wave, and this is true also of patients with aortic insufficiency, as demonstrated by records of sundry authors and our own.

In these patients we have, therefore, a double centrifugal wave, interrupted by a short phase in which the blood has lower pressure and lower speed, in spite of its centrifugal direction. The compression exerted by the stethoscope does not fundamentally affect these facts except as follows: in the proximal section the obstacle increases the height of the main wave, the depth of the predicrotic notch, and the height of the dicrotic wave; in the distal section, on the contrary, only the main wave is still present, for the dicrotic wave has been flattened. In other words, the optimal pressure to cause the second murmur is that which allows free passage to the top of the main wave, but blocks the flow of blood during the predicrotic notch. When the dicrotic wave meets the obstacle, it rises in height, and then filters gradually below it, and loses its individuality. When the blood at the level of the dicrotic wave meets the conical end of the artery above the compression, it forms eddies, and a murmur arises. As this blood filters gradually under the compression, the individuality of the wave is lost. No real murmur is recorded in a more peripheral section if the compression is extended over a long stretch. This explanation is confirmed by the fact that, when the main wave has a double top, separated by a depression (anacrotism), a double murmur occurs in the first phase, followed by a later murmur in the second phase. Complex polycrotic pulse waves sometimes produce a complex stethogram, with more short murmurs in the second phase.

Complete distal occlusion of the artery would prevent a centrifugal course of the main wave. This wave would still cause a first murmur under the stethoscope. After it, however, a slow backward flow, meeting more and more blood arriving from the center, would cause turbulent eddies, but no definite flow and no second murmur.

We shall now discuss the affirmed fact that the second murmur is increased by a distal compression, and that the first murmur is increased by a proximal one. As a matter of fact, only the first part is true, because the first murmur is increased by either a proximal or a distal compression. The reason is simple. The first murmur is caused by a large pulse wave, the main wave. Even passing under a compression, the blood flow is not markedly decreased, so that it is still able to cause

eddies after the obstacle. On the contrary, the second murmur is caused by the dicrotic wave, which is smaller and less sharp. As it meets the obstacle it becomes flat and nearly disappears, so that no appreciable eddies are formed after the obstacle.

The explanation of Pasoli,[16] who attributed the second murmur to arterial contraction, cannot be either proved or disproved here. If a tonic reaction occurs in the peripheral arteries and moves toward the periphery following the dilatation caused by the main wave (Hürthle,[8] Mareš,[14] Roncato,[19] Luisada[10, 11, 13]), this is likely to occur in the phase of the predicrotic notch. The peripheral progression of this reaction would increase the height of the dicrotic wave. Every obstacle causing a higher main wave, a deeper predicrotic notch, and a rise of the dicrotic wave would be accompanied by a stronger tonic reaction. Therefore, the second murmur of Duroziez can be explained by the theory of peripheral arterial contraction, but also in a much simpler way, as shown above.

The explanation of the second murmur in patients without aortic insufficiency is similar to that now advocated for patients with aortic insufficiency. The reason why Duroziez's sign is much more frequent in patients with aortic insufficiency than in others is very simple, and has already been advanced for many other arterial signs of aortic regurgitation.

High pulse pressure and high centrifugal speed of the pulse wave are found in the following conditions: (a) aortic regurgitation; (b) aortitis and atherosclerosis of the aorta without incompetence of the aortic valve; (c) hypertension; (d) hyperthyroidism; (e) fever. In most of these patients there is also a high dicrotic wave, in spite of the traditional belief that the dicrotic wave is very small in patients with aortic regurgitation. As a matter of fact, the point is that the rapid collapse of the arterial wall makes an exact record of the dicrotic wave more difficult to obtain in such patients. High speed and a high dicrotic wave also occur in cases of anemia.

The same categories of patients show Duroziez's sign in a decreasing order of frequency. Drugs which increase the pulse pressure and the tonic reaction of the arteries, like adrenalin, may cause the appearance of the double murmur in normal people.

In conclusion, the second murmur is caused by a centrifugal flow of blood, that of the dicrotic wave, which meets an obstacle and slowly passes below it. The old idea of Toussaint and Colrat[21] is, therefore, confirmed. The theory of backward flow is disproved by the following facts:

a. No deformity of the normal pulse curve is caused by the obstacle in the section where the murmur arises.

b. No deformity of the pulse curve is caused by the obstacle in the distant parts of the arterial tree.

c. No distal precession of the murmur is found when it is recorded simultaneously in two sections of the same artery.

The second murmur is often replaced, on records, by a sound, snap, or tone. This has exactly the same phase in comparison with the pulse wave as the second murmur. The mechanism of its production is similar to that of the second murmur, but not identical. The dicrotic wave meets with a section of artery which is completely occluded, and causes a snap of the wall. However, this cannot be the explanation of the sign of Traube. The double sound described by him occurs only rarely, and only when a slight compression of the stethoscope is exerted. The explanation of Traube, namely, that of a double snapping of the arterial wall suddenly dilating and suddenly collapsing, seems logical and still valid.

SUMMARY

1. A graphic study was made of the double murmur of Duroziez. Phonoarteriograms, electrosphygmograms, and other tracings were recorded on patients with aortic insufficiency and on others who had the clinical sign of a double arterial murmur upon compression.

2. The exact phase of occurrence of the second murmur has been ascertained. This is at the time of the predicrotic notch.

3. The best external pressure for the appearance of the second murmur has been studied. This is about three-fourths of the pulse pressure above the diastolic pressure, and coincides approximately with the level of the depression preceding the dicrotic wave.

4. The second murmur also occurs without compression at a certain point if compression similar to that reported above is made on a more distal section of the artery.

5. The obstacle presented either by the stethoscope bell or by a pneumatic cuff causes different changes above and below. Above the obstacle the predicrotic notch becomes deeper and the dicrotic wave becomes higher. Below the obstacle the dicrotic wave is more flattened, and may disappear. Above the obstacle the second murmur is sharp and distinct. Below the obstacle the murmur is either indistinct, or is represented by a dull snap, or is missing. This was true in patients both with and without aortic insufficiency.

6. The pulse tracing fails to reveal any abnormal deformity at the site of appearance of the second murmur. Also no deformity is found in the more peripheral pulse, in spite of the fact that the phase of appearance of the second murmur is often near the top of the main wave in the dorsalis pedis artery.

7. Simultaneous stethographic records at two points on the same artery fail to show an earlier appearance of the second murmur in the more distal section. As a matter of fact, they show a later appearance in that section, which demonstrates a peripheral blood flow during the occurrence of the second murmur.

8. Drugs which stimulate the circulation may cause the appearance of the double murmur of Duroziez in normal persons.

9. For all of the preceding reasons, a backward flow of blood during the second arterial murmur is denied, and a forward flow is admitted. The conditions of appearance are discussed, and a common explanation of the mechanism is furnished for both patients with and without aortic insufficiency.

10. The mechanism by which the sign of Traube is produced is further discussed.

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A FREQUENT OBSTRUCTIVE ANOMALY OF THE MOUTH OF THE LEFT COMMON ILIAC VEIN

WILLIAM E. EHRICH, M.D., AND EDWARD B. KRUMBHAAR, M.D.
PHILADELPHIA, PA.

WHEN performing an autopsy, one of the last acts of the pathologist is to open and inspect the inferior vena cava and its tributaries. He first opens the right common iliac vein and then approaches the left. Although the right is usually easily opened, the left at times is difficult to enter, not only because of its position behind the origin of the right iliac artery, but because, as we have found, the mouth of the left common iliac vein is frequently obstructed by fibrous thickenings and adhesions. Since this anomaly is not generally known, but seems to be important in regard to thrombosis of the lower extremities, which is known to occur more frequently in the left than in the right leg, a study has been made, on unselected material, of the structure of the inferior vena cava and its bifurcation into the two common iliac veins.

Literature.—The literature on the pathology of the inferior vena cava and its tributaries deals chiefly with malformations resulting from improper formation or obliteration of the posterior and supracardinal veins. Obstruction of the mouth of the left common iliac vein seems to have been described only by McMurrich,[1, 2] in 1906. If this observation remained unrecognized, it was probably because of the fact that the description was published only in abstract form.

In his second, more detailed, abstract, McMurrich states that he found an obstruction in 30 per cent of fifty-seven cases, and, with one exception, the lesion was in the left vein. There were three general types of obstruction, namely: (1) "A narrow thickening at the lateral border of the vein"; (2) a triangular adhesion at the lateral border of the vein, the base corresponding to the border, and the apex projecting toward the lumen; and (3) a columnar adhesion dividing the lumen into two portions and "occurring anywhere from the center of the lumen of the vein to within a millimeter or so of its lateral border." In one case an obstruction was observed in the right common iliac vein, and the lumen was double for a considerable portion of its course.

Considering the cause of the obstruction, McMurrich expressed the view that it seemed probable that it was a persistence of an embryonic condition. However, the relation of the lesions found to the ages of the subjects was not considered. As to the significance of the condition, he pointed to the fact that thrombosis of the iliac vein is much more frequent on the left than on the right side, and concluded "that in this adhesion may be found one of the contributory causes of the thrombosis."

From the Department of Pathology of the Medical School, University of Pennsylvania, and the Laboratories of the Philadelphia General Hospital.
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MATERIAL

After happening upon an obstructive lesion of the orifice of the left iliac vein (Autopsy 40789, Philadelphia General Hospital), and shortly after observing six additional cases among twenty-seven consecutive autopsies performed by the senior author, we undertook a systematic study of normal and obstructed iliac veins at various ages.

The veins were largely collected from the Philadelphia General Hospital but also from the Departments of Anatomy (Dr. Batson) and Pathology of the University of Pennsylvania. Included in this series was a case of situs inversus of the lower vena cava (Autopsy 41870, Philadelphia General Hospital), and eleven adult cases which were used for microscopic study only.

The total number of veins studied by us amounted to 412. Of these, 264 were from adults, 23 from adolescents 10 to 20 years of age, 28 from children 1 to 9 years of age, and 97 from stillborn babies and infants ranging from 21 cm. in length (vertex to coccyx) to 10 months of age.

OBSERVATIONS

Of the 399 of these 412 veins that were suitable for statistical analysis, 282 (70.5 per cent) had an essentially normal appearance, 95 (23.8 per cent) showed definite obstructive anomalies, 16 (4.0 per cent) were possibly slightly obstructed, and 7 (1.8 per cent) presented some other changes.

Normal Appearance of the Opening of the Left Common Iliac Vein Into the Vena Cava.—Of 261 essentially normal veins which were studied by us in detail, 215 showed a valve at the lower pole of the mouth (Fig. 1). In the remaining 46 veins the valve was lacking; its absence was observed in:

0 of 79	stillborn babies and small infants	(0 per cent)
6 of 35	children from 1 to 16 years of age	(17.1 per cent)
6 of 51	adults from 19 to 49 years of age	(11.7 per cent)
18 of 63	adults from 50 to 69 years of age	(28.6 per cent)
16 of 33	adults from 70 to 90 years of age	(48.5 per cent)
46		

A similar age distribution was found among 118 cases in which there were obstructive lesions, possible obstructive lesions, and other changes. In these cases, the valve was absent in 44:

1 of 18	stillborn babies and small infants	(5.5 per cent)
3 of 14	children from 1 to 16 years of age	(21.4 per cent)
13 of 33	adults from 19 to 49 years of age	(39.3 per cent)
15 of 36	adults from 50 to 69 years of age	(41.7 per cent)
12 of 17	adults from 70 to 90 years of age	(70.6 per cent)
44		

Textbooks of anatomy and pathology rarely give information about a valve at this point; some say that there is none, and others that it may sometimes be found. Our figures can be taken only to indicate that there is normally a valve at the mouth of the left common iliac vein, and that it is "worn off" in many persons with advancing age, and presumably worn down in still more. Now, if this valve is worn down, there is good reason to believe that other valves, such as those of the femoral veins, may also be worn down. This is significant in regard to the cause of varices of the lower extremities, which are often explained as a result of venous valvular insufficiency.

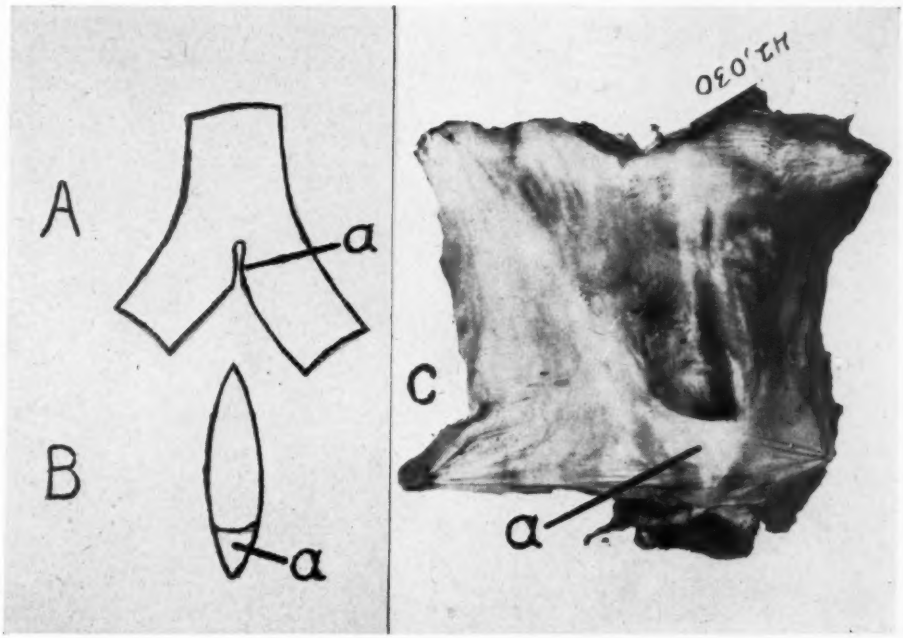


Fig. 1.—Normal opening of left common iliac vein into the inferior vena cava, with valve at lower pole (*a*). *A*, Anteroposterior view; *B* and *C*, lateral view (after opening inferior cava and right iliac vein) towards mouth of left common iliac.

The "Width" of the Orifice of the Left Common Iliac Vein.—This was ascertained by measuring the length of the longest axis; the orifice was held open by a pair of compasses without more traction than that required to get a smooth surface. This measurement was found to rise from about 2.5 mm. in the fetus measuring 21 cm. from vertex to coccyx, to about 7 mm. in stillborn babies measuring 40 cm. (Fig. 2*A*). After birth, it rose at first rapidly and later more slowly, to 20 mm. at about 15 years of age, and 24 mm. during the seventh decade. Thereafter it declined again (Fig. 2*B*). The fact that four infants from 1 to 2½ months of age showed a considerably smaller width than others of their age is obviously due to premature birth of these babies. This could be

confirmed in the case of one infant, 1½ months of age, which was only 30 cm. long (vertex to coccyx), for this is the length of the fetus in the eighth intrauterine month.

It may be mentioned here that there were no differences in the width of the mouth of the left common iliac vein or in the frequency of absence of the valve in relation to the subject's color or sex.

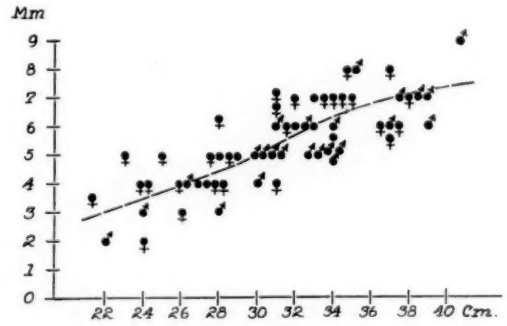


Fig. 2*A*.

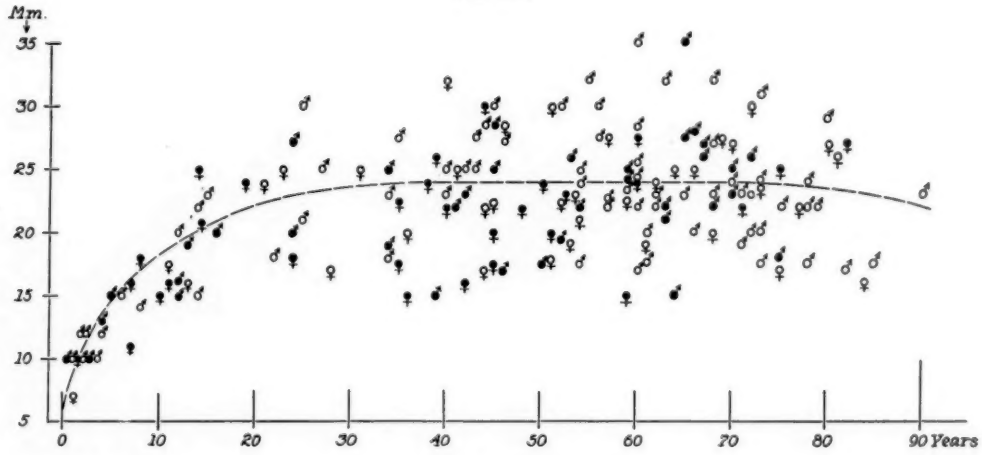


Fig. 2*B*.

Figs. 2*A* and 2*B*.—Chart of the width of the mouth of the left common iliac vein in relation to sex, color, and age. (*A*, In fetal life; *B*, in children and adults. In the latter curve, *B*, the open white symbols refer to white people, and the solid black circles to Negroes; whereas, in curve *A*, the white circles refer to both white people and Negroes.)

The Morphologic Appearance of the Obstructing Lesion.—According to their localization and other criteria, the lesions could be divided into five groups. Group I showed all transitions from "a narrow thickening" to triangularly shaped areas obstructing the upper pole of the mouth (Figs. 3, *I* and 4, *I*). Group II showed essentially the same picture except that all exhibited a channel passing along the left wall of the vein (Figs. 3, *II* and 4, *II*); and some also had one or several additional channels passing through the main portion of the obstructing

lesion (Figs. 3, *II* and 4, *II*). Group III included several varieties of adhesions dividing the lumen into two more or less equal portions (Figs. 3, *III* and 4, *III*). Some of these showed narrow bands (Fig. 3, *III*), whereas others showed membranes or triangular areas (Fig. 3, *III*). The latter were arranged either in the plane of the orifice (Fig. 3, *III*, second from left), or were perpendicular to it (Fig. 3, *III*, fourth and

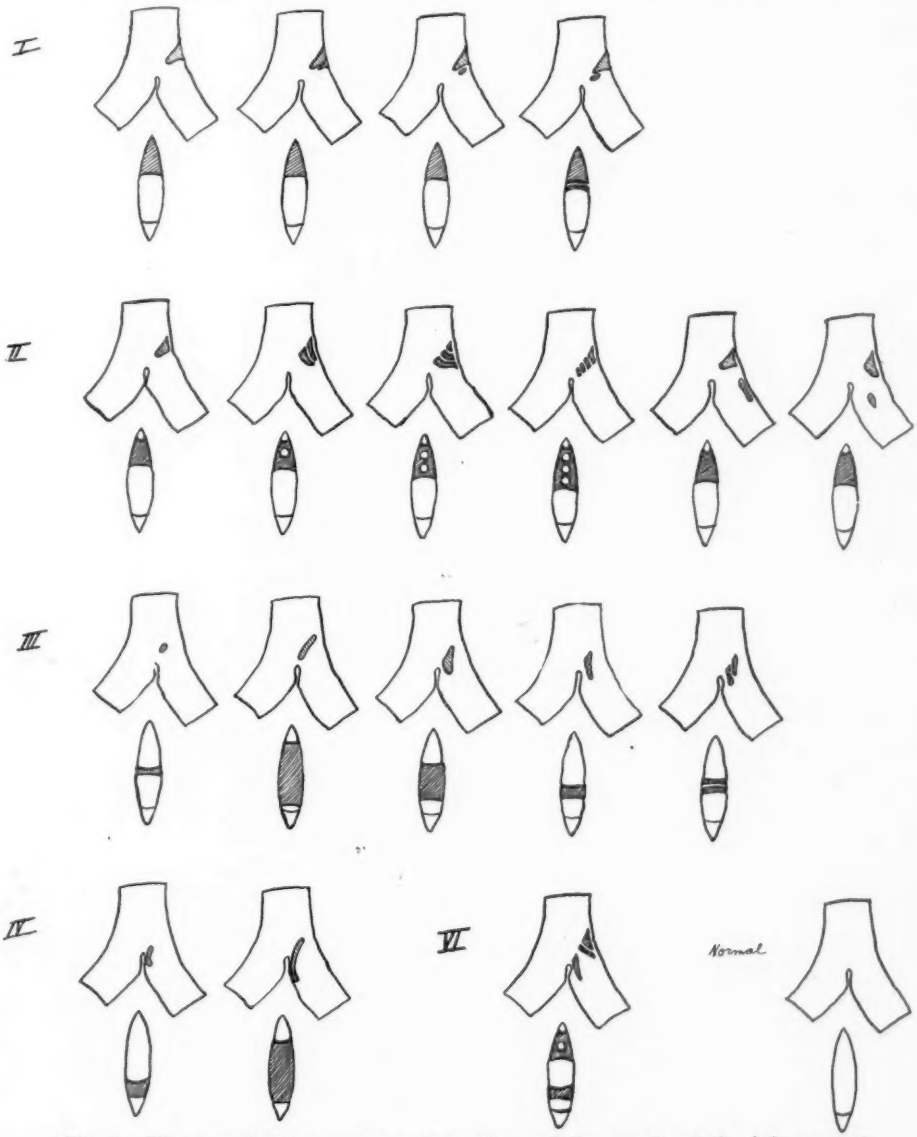


Fig. 3.—Diagram showing various obstructions of the mouth of the left common iliac vein as seen in the anteroposterior view and in the lateral view (from inferior cava and right iliac towards mouth). Nos. *I* to *IV* refer to the various groups of obstructions as described in the text: miscellaneous Group V obviously cannot be represented by a single figure; No. VI is a combination lesion of II and III.

fifth from left). Group IV included adhesions at the lower pole of the mouth, showing a tendency to extend behind the valve (Figs. 3, *IV* and 4, *IV*); and Group V included miscellaneous lesions, most of which were characterized by multiple irregular bands (Fig. 4, *V*); one showed such an extensive obliteration of the orifice that at no place could a probe be inserted, and water filtered through very slowly (Fig. 5, *B*). Yet just below the orifice the vein was patent and smooth-walled (diameter, 8 mm.). Some showed remnants of thrombotic material (Fig. 4, *Vx*). In one case, finally, a combination of Groups II and III was observed (Fig. 3, *VI*).

Of our obstructions, 38 belonged to Group I, 23 to Group II, 12 to Group III, 9 to Group IV, and 13 to Group V (Table I). The upper pole of the opening thus appears to be the seat of obstructions more frequently than the lower pole.

TABLE I

FREQUENCY OF THE VARIOUS OBSTRUCTIVE LESIONS, WITH FREQUENCY OF ABSENCE OF VALVE

TYPE OF OBSTRUCTION GROUP	WITH VALVE	WITHOUT VALVE	TOTAL
I	18	20	38
II	12	11	23
III	6	6	12
IV	8	1	9
V	5	8	13

The width of the lumen of the left common iliac vein immediately below the obstructions of the orifice was not materially altered by their presence, except in Autopsies 41397 and 41798, in which orifice and lumen were so narrow that a probe measuring 2 mm. in diameter could be forced through only with difficulty (Fig. 4, *Vy*). It can be assumed that this observation depends on such factors as the age at which the lesion became obstructive and the nature of the collateral circulation that developed.

There was no persistence of a left posterior cardinal vein or supracardinal vein in any of the cases in which this possibility was investigated.

As to the valve at the lower pole of the opening, Table I indicated that it was missing in 48 per cent to 58 per cent of the cases in all groups except Group IV, in which it was absent in only 11 per cent. The frequent absence of the valve in the presence of obstructions seems to be well explained by the greater stress and strain to which such a valve is exposed, and, in extreme cases, to obliteration of the valve by the sclerotic process. As to the less frequent absence of the valve in Group IV, aside from the small number of cases in this group, the explanation may be due, not to the youth of the persons involved, for the average age of this group amounted to over 60 years, but to the fact that the

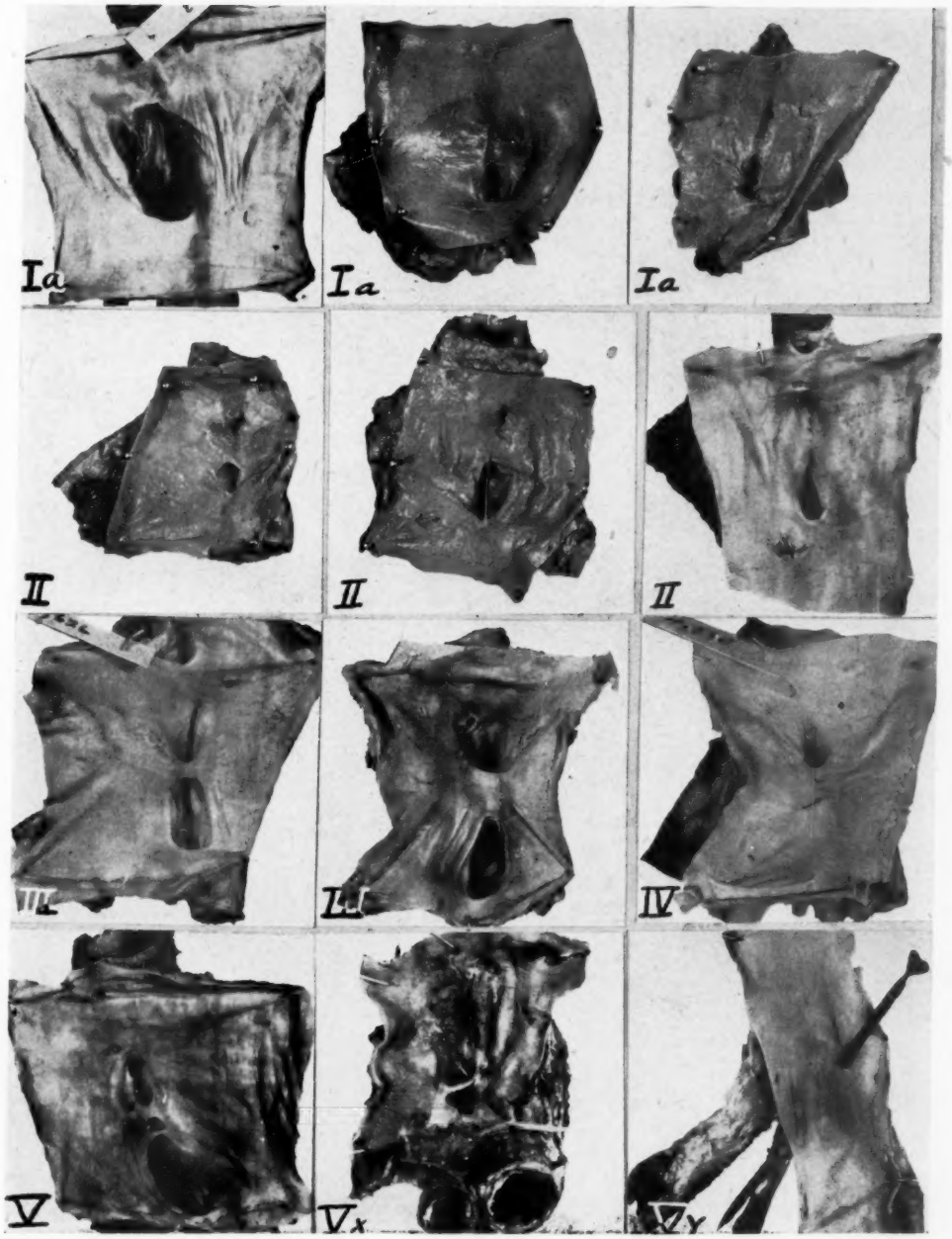


Fig. 4.—Various obstructions of the mouth of the left common iliac vein as seen in the lateral view. Nos. I to V refer to the various groups of obstructions as described in the text.

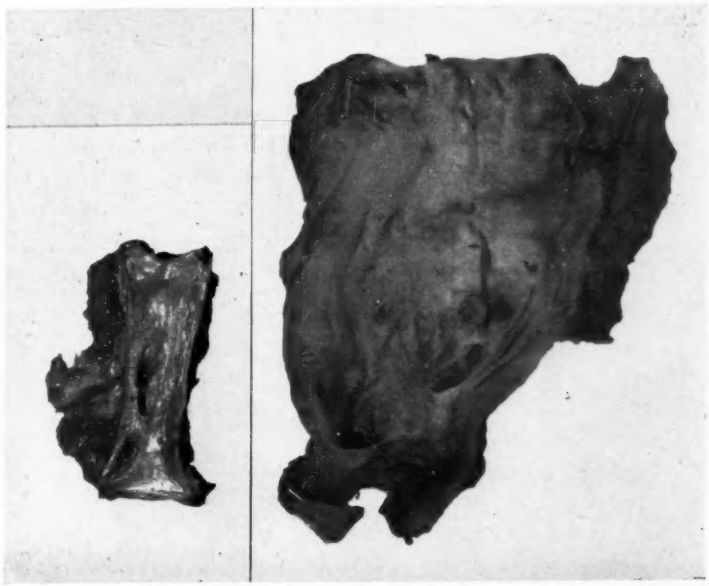
TABLE II

AGE DISTRIBUTION OF THE VARIOUS OBSTRUCTIVE LESIONS IN 95 INSTANCES IN WHICH AGE WAS KNOWN

TYPE OF OBSTRUCTION / GROUP NO. / AGE PERIOD	AGE PERIODS										TOTAL
	MONTHS	YEARS									
	0-12	1-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80 ON	
I	0	1	3	3	3	7	5	8	4	4	38
II	2	0	2	3	3	4	2	4	3	0	23
III	1	1	0	0	0	2	2	4	2	0	12
IV	1	0	0	0	1	1	0	2	3	1	9
V	0	1	3	0	1	2	4	1	0	1	13
All groups	4	2	9	6	8	16	13	19	12	6	95
	6		89								
Number of veins examined of known age	97	30	22	15	21	50	43	57	39	16	390
	127		263								
Percentage of cases studied	4.1	6.7	40.9	40.0	38.6	32.0	30.2	33.3	30.8	37.5	
	4.7		33.8								

obstructing lesion in Group IV stands in the way of the bloodstream, which exerts stress and strain on the valve; that is to say, the valve is protected by the lesion. That this may be the correct explanation seems to be borne out by the fact that absence of the valve in this group occurred even less often than in our normal subjects of similar age (see figures in paragraph on the normal appearance).

Histology.—The microscopic appearance of our lesion seemed to be the same in most cases. There was a great deal of elastic tissue, and some collagenous tissue; smooth muscle cells were also present. On the other hand, inflammatory cell infiltrations were not observed, nor was the irregular arrangement of scar tissue found.



A. *B.*

Fig. 5.—*A*, Obstruction of the mouth of the left common iliac vein in a newborn baby measuring 31 cms. in length (Group III, No. 9). *B*, Obstruction so great that probe could not be inserted and water barely filtered through (male, 9 years of age, University of Pennsylvania Hospital, Autopsy '43—318).

The Age Distribution of the Obstructing Lesion.—After the first decade, the obstructing lesion was found in 33.8 per cent of all our cases (Table II). There was no significant difference in incidence of obstruction between any of these age groups after the first decade, and there was no significant age difference in the relative frequency of the obstructions analyzed according to groups. Among our stillborn babies and children up to 10 years of age, we found only six cases (4.7 per cent) of definite obstructions. These belonged to Groups I, II, III (Fig. 5), and IV. However, in this group of stillborn babies and children up to 10 years of age, sixteen possible obstructions were observed at the upper

pole of the orifice; the entries in the protocols read: "Probably adhesion at upper pole," "fold at upper pole resembling adhesion," etc. If we add these to our number, the frequency in stillborn babies and infants up to 10 months rises to 17 per cent, and that of children from 1 to 10 years, to 26.3 per cent. These small, delicate vessels must be seen to realize the difficulty in making correct decisions as to the presence or absence of obstruction.

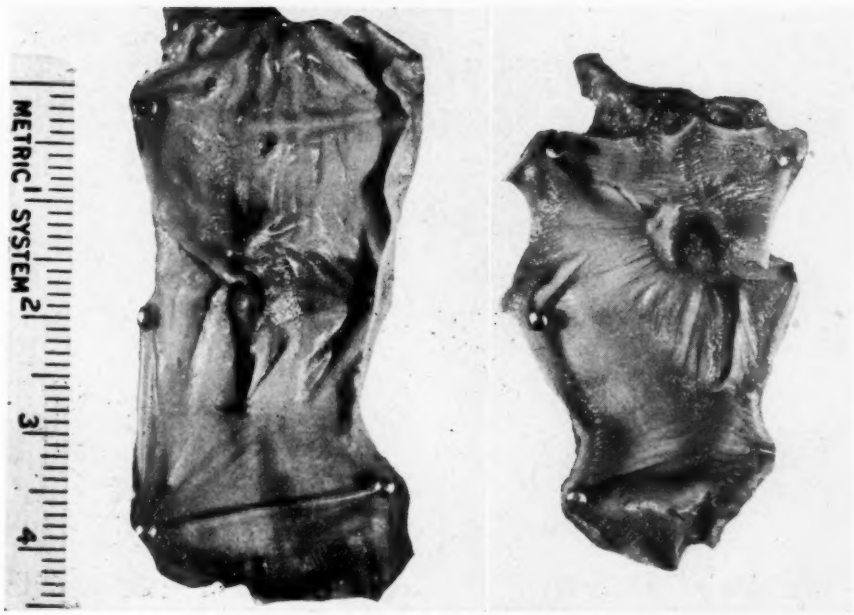
Other Anomalies.—Changes other than obstructive lesions which were observed among our cases were: (1) An unusually large valve with a perforation at its lower pole (Autopsy 41810, 43 years, female, Negro; Autopsy 42101, 67 years, male, white); (2) low position of the valve (Autopsy 16, body 24 cm. long, anencephalus); (3) an unusually low bifurcation with absence of the valve (Autopsy 42580, 2 years, male, Negro); (4) absence of the common portion of the left common iliac vein, with two mouths at the bifurcation (Autopsy 12, body 30 cm. long); (5) complete fibrous obstruction of the lower section of the inferior vena cava between its bifurcation and the mouths of the renal veins, with the posterior rami of the lumbar veins markedly distended, compensatorily (Autopsy 46217, 68 years, female, white); (6) adhesions in the right common iliac vein as a part of an organizing thrombus (Autopsy 41561, 49 years, female, Negro); and (7) situs inversus of the lower vena cava (Autopsy 41870, 66 years, male, white).

Although the anomalies listed here under numbers 1 to 5 do not appear to have received attention, both numbers 6 and 7 have been previously recorded. Adhesions in the right common iliac vein were seen once by McMurrich,[1, 2] and situs inversus of the lower vena cava has been observed by a good many authors. Zumstein[3] found situs inversus in 0.45 per cent of his cases, and Seib,[5] in 0.56 per cent (for literature see Maxwell and Erwin[4] and Seib[5]).

DISCUSSION

If we compare our observations with those of McMurrich, we find conformity as far as the frequency of the obstructions is concerned. Whereas McMurrich[2] observed a frequency of 28 per cent (in 57 cases), we found an incidence of 4 per cent to 17 per cent in babies up to 10 months of age; 9.7 per cent to 26 per cent in children from 1 to 8 years; and 33.6 per cent in all age groups beyond 10 years. (N. B. The wide range given in the younger groups is influenced by the large personal factor which enters into the decision when the veins are very small and flexible.) As to the morphology of the obstructions, our Group I corresponded to McMurrich's Types 1 and 2, and his Type 3 embraced our Groups II and III. Our Groups IV and V were not described by McMurrich.

Concerning the pathogenesis of the obstructions, McMurrich's idea[1] that they are probably the result of defective embryonic development



A. *B.*

Fig. 6.—Recent obstructions of the upper pole of the mouth of the left common iliac vein in children 10 and 13 years old (Autopsies 43881 and 1056).

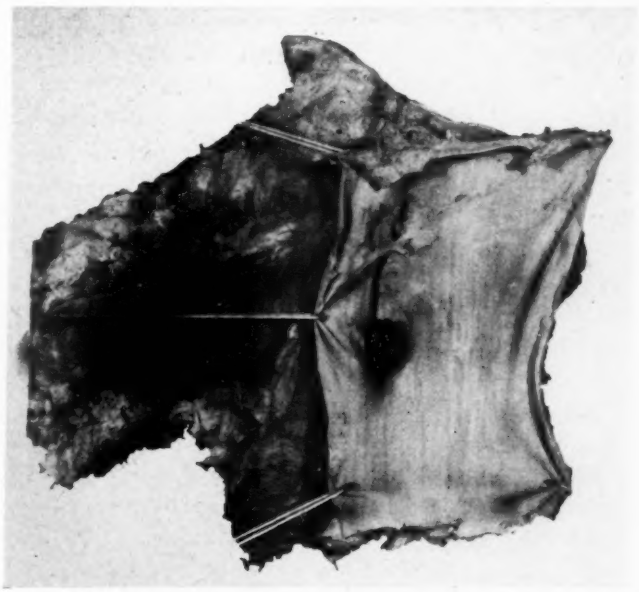


Fig. 7.—Thrombosis of the left common iliac vein in a case of obstruction of the greater portion of the mouth (Philadelphia General Hospital, Autopsy 41493).

is of interest in view of the closure of several segments of the left cardinal vein and the union of the left iliac with the vena cava by means of a developing communicating branch. The view is not supported, however, by our observations that only a few clearly developed obstructions are seen in the newborn and in children up to 10 years, whereas adhesions *in statu nascendi* were found in children as old as 10 or 13 years (Fig. 6). As a matter of fact, our observations seem to show that relatively few obstructions are formed during embryonic life, and that the great majority arise after birth. But since the frequency of adhesions in the second decade was as high as in the adult group, it may be concluded, with due regard to the small numbers available in the separate age groups, that most obstructions are acquired during development and growth, and that few, if any, are formed after the second decade.

As to the cause of the obstructions, it should be noted that most were located at a point where the right iliac artery crosses and exerts pressure on the left iliac vein. It is conceivable that this pressure interferes with the proper development of its orifice or causes an injury resulting in organization and fibrosis. (It should be noted, in evaluating this factor, that the relative positions of the arterial and venous bifurcations may change with age, and may be different during life from what they are on the autopsy table, according to the law that an elastic tube lengthens, as well as dilates, with increasing pressure.) That this pressure factor may be the correct explanation is further supported by the observation that no such obstructions have been found at the mouth of the left renal vein, the embryonic development of which from a segment of the left cardinal vein closely resembles that of the left common iliac; but here the aorta lies behind the vein.

Some of our obstructions were found to be organized thrombi. These are included in our Group V, although in not all cases of this group was the obstruction the outcome of thrombosis. Obstructions as a result of organization of thrombi differ from other obstructions in that they lack a definite pattern, show great irregularity in the arrangement of the individual bands of connective tissue, and show various transitions from early thrombosis to complete organization. In this group should be included, also, our only case of right-sided obstruction, for the thrombus which caused the proliferation of the connective tissue could still be identified.

Considering the clinical significance of our observations, we wish to discuss briefly the occurrence of thrombi in the iliac veins. Thrombosis in this location was observed in nine of our adult cases. In seven cases we found involvement only of the left side (Fig. 7); whereas, in the two remaining cases, both sides were involved. Of the seven cases in which there were thrombi in the left vein, there was partial obstruction of the orifice in four, and no obstruction in three. Since we have found that absence of this obstruction in adults is twice as common as its pres-

ence, it follows that, in our material, thrombosis of the left common iliac vein was more than twice as common in cases of obstruction than in those in which there was no obstruction.

In order to study this matter in larger numbers, the records of 1,000 consecutive recent autopsies at one of our hospitals were examined. In this series, pulmonary embolism was recorded 82 times. In these 82 cases, iliac vein thrombi were found 11 times. Furthermore, in 16 cases in which iliac vein thrombosis was recorded (in some of which there was no pulmonary embolism), the right common iliac vein was found to be affected 3 times; the left, 8 times; and both veins, 5 times. These figures show once more the preponderance of thrombosis in the left common iliac vein.

SUMMARY

This study of the opening of the left common iliac vein into the inferior vena cava is based on the examination of 412 bodies: 97 stillborn babies and infants up to 10 months old, 28 children from 1 to 9 years of age, 23 adolescents from 10 to 19 years of age, and 264 adults up to 90 years of age.

The width of the opening first increased rapidly with increasing age, and later more slowly. The curve reached its peak during the seventh decade.

A valve was found to be normally present in the newborn at the lower pole of the opening, but it appeared to be worn off in an ever greater percentage as age progressed, and more so in obstructed than in normal openings. This observation seems to be significant with regard to the cause of varices of the lower extremities, which have often been explained as a result of venous valvular insufficiency.

Obstruction of the orifice in the 399 cases analyzed was observed in 95 instances (23.8 per cent), with a possibility of 16 more instances in the stillborn and infants. It was less common in children and babies (4.7 per cent), although, if the 16 doubtful cases are included, the percentage rises to 17.3 per cent. In those over 10 years of age, it was found 89 times (33.8 per cent). It occurred with equal frequency in males and females, and in whites and Negroes.

According to location and other criteria, the obstructions could be divided into five groups (Figs. 3 and 4). The most common site of obstruction was the upper pole of the orifice, where two-thirds of all obstructions were found.

Concerning the pathogenesis of the obstructions, few, if any, were thought to be caused by faulty development, per se. They appeared to be acquired during the growth period, rarely before birth, and rarely after adolescence.

As to the mechanism involved, it was observed that the obstructions occurred at a point where the right iliac artery crosses and exerts pressure on the vein. This pressure conceivably interferes with the proper development of the opening into the vena cava or causes an injury resulting in organization and fibrosis. In a small number of cases the obstructions could be shown to be organized thrombi.

The clinical significance of the obstructions is apparent from the greater frequency of thrombosis in the left than in the right leg. This preponderance could be confirmed in our material, as well as in an analysis of 1,000 consecutive autopsies from one of our hospitals.

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DISSEMINATED ARTERIAL INTIMAL PROLIFERATION, WITH THROMBOSIS

Report of a Case

Kenneth C. Kehl, M.D., and Gorton Ritchie, M.D.
Racine, Wis.

In 1879, von Winiwarter[1] described a disease of the peripheral arteries which he termed "endarteritis obliterans." Since that time a voluminous literature on the subject of vascular occlusive diseases has accumulated, and various theories have developed concerning the pathogenesis and essential nature of the lesion. In 1908, Buerger[2] criticized the term "endarteritis obliterans" and described a condition which he called thromboangiitis obliterans, outlining certain diagnostic criteria. Other authors, however, have since included under this name conditions which do not fulfill these criteria. It seems possible, therefore, that the term thromboangiitis obliterans has been used to denote more than one disease entity, and, consequently, the classification of vascular occlusive diseases has remained confused.

The present case belongs somewhere in this category, but, because of certain clinical and pathologic features, it defies accurate classification.

CASE REPORT

M. M., a 27-year-old, white housewife, was seen in March, 1941, when she complained of the symptoms commonly associated with congestive myocardial failure, namely, dyspnea, orthopnea, cough, hemoptysis, palpitation, tachycardia, pain in the chest, and edema. The onset of the present illness had been insidious, and much of the history prior to the first visit was obscure, except that she had consulted several physicians without definite improvement in her condition.

There was a history of diphtheria and a doubtful history of chorea during childhood. No history suggestive of rheumatic or scarlet fever could be obtained.

She had had dyspnea, palpitation, tachycardia, and peripheral edema of such severity as to necessitate rest in bed for the first time, in May, 1939, about two years before our first visit, although she apparently had not been in good health for a considerable period prior to this incident. From that time until she was seen in March, 1941, the attacks of cardiac failure had recurred frequently, and had become more severe, more frequent, and more prolonged, in spite of all treatment. As the condition progressed, attacks of pain in the chest, fever, cough, and hemoptysis had occurred, and were usually followed by an increase in the degree of heart failure. She said that the heartbeat had been irregular at times.

From the Department of Medicine and the Clinical Laboratory, St. Mary's Hospital, Racine, Wis.

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Severe abdominal pain, associated with fever, distension, and obstinate constipation, had occurred on several occasions before she came under our care. The pain was described as having been diffuse, although in one instance it became localized in the left flank and left costovertebral region. A moderate leucocytosis was associated with this attack, but no significant urinary abnormalities were present at any time. Enemas and opiates afforded only moderate relief. Roentgenologic studies of the stomach and bowel at a later date revealed no evidence of disease, but a chest roentgenogram at that time was said to have shown cardiac enlargement, with a mitral contour.

On Feb. 21, 1941, during a period of hospitalization, she suddenly became very apprehensive and confused. At that time she gave evidence of difficulty in swallowing and talking, and complained of numbness of the left side of the face and body. The examiner noted muscular weakness of the left side of the face, left arm, and left leg. The information concerning this incident is incomplete, but, within thirty minutes, sensation had begun to return, and no evidence of residual weakness could be detected a few hours later.

The initial examination revealed a very apprehensive and restless white woman, with marked dyspnea and orthopnea. The skin was pale and the mucous membranes were cyanotic. The neck veins were distended and showed forceful pulsations. There was puffiness about the eyes. Râles were heard throughout both lungs, and the percussion note was dull over both lung bases, with diminished breath and voice sounds in those areas. The heart was enlarged to the left. The rhythm was regular and the rate was 120 per minute. The pulmonic second sound was accentuated. No murmurs could be heard. The blood pressure was 132/104. The edge of the liver was felt three fingerbreadths below the right costal margin in the midclavicular line. The abdomen was slightly distended, and there was dullness to percussion in the flanks. Pitting edema was present in the ankles and in the dependent portions of the legs and thighs. Urinalysis showed 1 plus albumin, occasional hyaline and granular casts, and occasional pus cells.

She was placed on a restricted fluid and salt intake, and was fully digitalized with a *Digitalis lanata* preparation (Cedilanid, Sandoz), but failed to show much improvement. Large doses of ammonium chloride, followed by a mercurial diuretic, produced a good diuresis, and the edema and respiratory distress diminished considerably. In spite of relatively large doses of digitalis and the use of sedatives throughout the day, the pulse rate remained rapid, ranging from 100 to 130 per minute throughout the greater part of her illness. However, with the use of ammonium chloride and the mercurial diuretic, the respiratory distress was greatly relieved, and only minimal edema was present. At this time a soft systolic murmur was heard at the apex, but soon disappeared. This murmur was occasionally present throughout the course of her illness.

About three weeks after the initial examination, when the heart was well compensated, and shortly after an intravenous injection of the mercurial diuretic, she developed a severe pain in the lower, right side of the thorax. This was followed by a rise in temperature to 101.6° F., cough, and hemoptysis. The dyspnea and cyanosis were increased. Examination of the chest revealed a new area of dullness in the right base, with absent breath sounds and voice sounds in that area. The accentuation of the pulmonic second sound had increased.

This attack was followed very promptly by a return to a state of marked congestive failure. It was regarded as reasonably certain that pulmonary infarction had occurred. Similar incidents occurred quite frequently during the course of her illness, usually when the cardiac failure had diminished. On each occasion the degree of failure increased markedly within a period of twenty-four hours after the onset of the pain.

In July, 1941, she developed pain in the left leg, followed by a marked increase in the edema of that leg, with some pallor of the skin. Since the patient was at home and notification was delayed, she was not seen until about thirty-six hours after the onset. Examination showed tenderness over the great vessels in the groin, and also in the popliteal space. There was no evident temperature difference between the two legs, and the reflexes, muscular movements, and sensations did not appear altered. The edema was so marked that it was questionable whether the dorsalis pedis and posterior tibial pulses were present. The femoral pulse was forceful in the groin, and, although of small volume, the popliteal pulse was present. The edema subsided gradually over a period of two weeks, and there was no evidence of muscular weakness or skin changes. The dorsalis pedis and posterior tibial pulses now were obviously present, but of small volume, and remained so throughout the course. It was thought that she had had thrombophlebitis.

In August, 1941, there was another cerebral attack like that which had occurred on Feb. 22, 1941. The anxiety and confusion were so marked that the patient cooperated very poorly. Swallowing and talking were found to be difficult, but on this occasion there were no paresthesias. Examination revealed no evidence of cranial or other nerve disturbances, nor were any sensory changes detected. Again the incident was very transitory.

About one month later, in September, 1941, an opportunity presented itself to observe her when she was suffering from the abdominal pain already described. The pain, which was very severe, was on this occasion located in both upper quadrants and did not radiate. It was associated with vomiting, marked gaseous distension, and obstinate constipation. The temperature was elevated to 99.4° F. on this occasion. No urinary symptoms could be elicited. The patient cooperated poorly, but the entire upper part of the abdomen seemed tender. The liver was enlarged, but the kidneys and spleen could not be felt, and no other masses could be made out. There was no definite flank or costovertebral tenderness. Urinalysis revealed 1 plus albumin, casts, and occasional leucocytes, but no erythrocytes. Opiates, external heat, and enemas gave only moderate relief, but within a week the pain had disappeared.

On Oct. 29, 1941, the abdominal pain recurred and became so severe that she consented to hospitalization, which she had refused persistently up to this time. The picture on this occasion was similar to that already described. The site of the abdominal pain was variable with each attack, and occasionally varied from day to day during a particular attack. Although never well localized, the pain most frequently occurred in one or both upper quadrants, and on occasion radiated into the chest.

During her hospitalization, repeated attacks of chest and abdominal pain occurred, at which times the temperature was usually elevated, occasionally rising to 102° F. The pulse rate varied from 90 to 130

per minute. At all times there was some evidence of cardiac failure, although ammonium chloride, followed by large doses of mercurial diuretics intravenously, reduced the edema and respiratory embarrassment for short periods. At times during the course there was considerable facial edema, and on two occasions marked anasarca developed. By this time the heart had increased considerably in size and the accentuation of the pulmonic second sound had become much more marked.

An electrocardiogram taken Nov. 3, 1941, revealed normal sinus rhythm, with a rate of 104 per minute. The P-R interval was prolonged to 0.22 second. The QRS interval was 0.09 second. P_2 was of 0.12 second duration, and of greater voltage than QRS_2. QRS was of low voltage and slurred in all leads. The first ventricular complex consisted of a positive deflection alone in Lead I, and a barely perceptible positive deflection, followed by a negative deflection of 3 mm., in Lead III. QRS_2 was of the M-type, and almost isoelectric. $S\text{-}T_1$ was very slightly depressed, and followed by an erect T_1 of very low voltage. T_2 was isoelectric. $S\text{-}T_3$ was isoelectric, and followed by an inverted T_3 of very low voltage. QRS_4 was diphasic. $S\text{-}T_4$ was elevated 2 mm., with an isoelectric T_4. The negative deflection of QRS_4 was slurred. This record was felt to indicate extensive myocardial damage, with first degree A-V block and probably a myocardial infarct.

A roentgenogram of the chest taken Nov. 7, 1941, showed marked enlargement of the cardiac shadow, without any typical pathologic configuration. There were residual interstitial changes in the upper and lower portions of the right lung which were compatible with resolving infarcts.

Laboratory studies during her hospitalization gave the following results: The blood Kahn reaction was negative. The hemoglobin was 13 Gm., the erythrocyte count, 3,930,000, and the leucocyte count, 10,700; a differential leucocyte count showed 7 per cent stab forms, 74 per cent segmented forms, 18 per cent lymphocytes, and 1 per cent monocytes. A blood smear showed polychromatophilia and occasional nucleated erythrocytes. Urinalysis showed a specific gravity from 1.005 to 1.017, albumin from 0 to 4 plus, no sugar, no acetone, hyaline and granular casts, 1 plus epithelial cells, 2 to 4 leucocytes per high-power field, and no erythrocytes. The blood nonprotein nitrogen was 60 mg./100 c.c. The serum protein was 5.4 per cent.

On Nov. 8, 1941, the edema of the legs increased very rapidly to such an extent that the skin over the entire legs, and especially below the knees, became tense and shiny. At this time she complained of heaviness in the legs and of awkwardness of motion, but there was no pain. On the next day both legs felt numb, and they now appeared pale and slightly cyanotic. The reflexes were found to be present, but sluggish. There was no evidence of sensory disturbance, although the extremities felt cold to the touch and the pulses could not be felt. As the massive edema subsided over a period of several days, the popliteal, posterior tibial, and dorsalis pedis pulses could again be made out bilaterally, although they remained of small volume. Bilateral arterial occlusion of the lower extremities was considered at this time, but was thought to be unlikely because of the return of the pulses and the failure of gangrene to develop.

On Dec. 5, 1941, two nodules about 1 cm. in diameter were noted on the extensor surface of the left forearm. These were slightly movable and slightly tender to the touch. Three days later a similar nodule

appeared in the right cheek, and was attended by slight swelling. In each case the nodules persisted for about five days and then disappeared quite rapidly.

Her condition became progressively worse from this time on. The respiratory embarrassment and edema became more marked, and she required more frequent and larger doses of mercurial diuretic for even moderate relief. Either thoracic or abdominal pain was experienced almost daily at this time. She became increasingly uncooperative, and finally became irrational, and died Jan. 9, 1942.

Summary of Clinical Observations.—A 27-year-old white woman, with a past history of diphtheria and a doubtful history of chorea, suffered from an undiagnosed cardiovascular disease for at least two and a half years, and probably longer. Her illness was marked by dyspnea, orthopnea, cough, and edema. The size of her heart increased during the illness. Occasionally a transient, soft, systolic murmur was heard at the apex, and the accentuation of the pulmonic second sound became more marked. The electrocardiogram showed evidence of extensive myocardial damage. Repeated attacks of thoracic pain, fever, cough, and hemoptysis were considered to be caused by pulmonary infarction. Severe abdominal pain, gaseous distension, and obstinate constipation occurred repeatedly, without urinary symptoms or tenderness over the kidneys. Two cerebral seizures, marked by difficulty in talking and swallowing, confusion, apprehension, anxiety, and transient neurologic disturbances, occurred. The sudden increase in the edema of the lower extremities on two occasions was thought to be caused by peripheral vascular occlusion. The patient ultimately failed to respond to therapy.

AUTOPSY

The body was that of a poorly nourished white woman whose apparent and actual age were approximately the same. The veins of the neck were dilated, an old appendectomy scar was present, and the left ankle was slightly edematous.

The peritoneal cavity contained a small amount of excess fluid, and a few fibrous adhesions were present at the site of the appendectomy. No constriction of the bowel was noted. The left pleural cavity contained about 150 c.c. of clear yellow fluid, and the right cavity, a small amount of the same fluid. Many fibrous adhesions were present in the right pleural cavity. The pericardial cavity contained 200 c.c. of clear fluid.

The heart weighed 460 grams. Irregular patches of scar tissue were present in the myocardium; the largest of these was in the wall of the left ventricle near the apex, and measured 5 mm. in diameter. The valves were soft and thin. On the endocardium of the left ventricle there were many thrombi of all ages. A few of these were seen in the right ventricle also. In the right auricular appendage there was a thrombus 5 cm. in diameter which not only filled the appendage, but also extended out over the tricuspid orifice as a pedunculated mass. The coronary arteries were thin walled, and no evidence of occlusion could be found grossly.

The lungs showed some generalized thickening of the framework, and a large number of infarcts of all ages were seen. The large pulmonary arteries were grossly patent.

The right kidney weighed 100 grams. The capsule was slightly adherent and the surface was congested, with many depressed areas

The cut surface was unremarkable except that many infarcts in various stages of healing were seen. The left kidney was similar to the right.

The aorta was elastic, and its intima was smooth down to about 8 cm. above the bifurcation. Extending from here downward and into the iliac arteries there was a thrombus. Its aortic portion was mural in character; it was situated on the posterior wall of the vessel, and was very pale and firmly attached to the intima. In its iliac portion it occluded the vessels entirely, and varied in structure, i.e., it was red in some portions and somewhat decolorized in others. The veins were entirely patent.

MICROSCOPIC OBSERVATIONS

Heart.—Some hypertrophy of the muscle was present, and there was extensive patchy fibrosis, giving the impression of infarction with healing. The coronary arteries did not appear thickened, and no coronary thrombus could be found. The endocardial thrombus was of various ages in various parts, from a few days in the superficial layers to much longer in the deeper portions, in which there was thorough organization. The structure was typical of a laminated thrombus with organization.

Lungs.—There was chronic passive congestion. The lung framework was greatly thickened. Many infarcts were present; some of these were fairly fresh, but most were in various stages of encapsulation or organization. The arteries were the site of intimal thickening, and a large number were occluded by organized and canalized thrombi. The newly formed vessels in these thrombi were of considerable size in many instances, with muscular walls and a definite elastic tissue component.

Spleen.—Chronic passive congestion, hyperplasia of the lymphoid follicles, and hyaline changes in the smaller arteries were the lesions found here.

The liver was the site of hydropic degeneration and chronic passive congestion. The gastrointestinal tract was the site of slight chronic inflammation in the mucosa.

Kidneys.—Multiple infarcts were present, some of which were fresh, some organizing. Intimal thickening and fibrosis were present in the small and medium-sized arteries, and extreme splitting of the internal elastica was seen in many areas. Organized and canalized thrombi were present in many of these arteries, and the canalizing vessels in some cases had developed fairly thick, partially muscular, walls. A careful search revealed no fresh thrombi.

Aorta.—Typical organized thrombus.

Iliac Arteries.—A fresh, red thrombus was present, with partial organization. The artery wall was approximately normal.

Summary of Pathologic Observations.—The heart was hypertrophic, and, although no coronary sclerosis or thrombosis was found, there were patchy myocardial scars and endocardial thrombi. The small and medium-sized arteries of the lungs and kidneys were the seat of intimal thickening and fibrosis, and in many of these vessels there were organized and canalized thrombi. Multiple infarcts of various ages were present in these organs. A thrombus was present in the lower part of the aorta and common iliac arteries. This was mural in character in the aortic portion, but completely occluded both common iliac arteries. In the aortic portion it was decolorized and or-

ganized, whereas the iliac portion was fairly fresh, with beginning organization. No inflammatory changes were found in the vessel walls or thrombi.

DISCUSSION

This case, although obviously one of generalized vascular disease, defied all attempts at specific clinical or pathologic diagnosis. The pathologic picture corresponded in some respects to that which some investigators have considered as characteristic of thromboangiitis obliterans. Hausner and Allen[3] found purely degenerative lesions in the visceral arteries, whereas the peripheral vessels showed the typical inflammatory changes of Buerger's disease. Fatheree and Hines[4] emphasized the generalized nature of the lesions, and stated that the characteristic inflammatory process occurred but rarely in the visceral arteries, and never without associated degenerative lesions.

Eppinger[5] regarded the salient features as (1) marked intimal proliferation, (2) extensive thrombosis with canalization, (3) remarkable preservation of the internal elastic membrane, and (4) relatively intact media and adventitia; he merely mentioned, in passing, the lymphocytic infiltration and edema of the media.

In Cabot Case No. 22102,[6] post-mortem examination revealed extensive, organized, and canalized thrombi in nearly all the medium-sized and small pulmonary arteries. These lesions were similar to those found in the present case, and this condition was considered by the pathologist to be endarteritis obliterans.

In a study of 200 cases, Telford and Stopford[7] came to the following conclusions: The first change is proliferation of the intima, probably as a result of vasospasm, followed later by thrombosis at the intimal irregularities. The thrombus increases by propagation. Three zones are then seen in a cross section of the artery: (1) the thickened intima, (2) organized thrombus material, and (3) fresh thrombus. When the thrombus extends centrally from the primary thrombus, cross section of the vessel may not show the intimal change. Later there may be fibrosis of the media and adventitia. They do not consider the organization to be of any peculiar type, and emphasize the absence of collections of lymphocytes.

Staemmler[8] described a case of diffuse disease of the pulmonary arteries, with intimal overgrowth, thrombosis, canalization, and reduplication and splitting of the internal elastica. No actual inflammatory lesions were found, but the author designated the condition as thromboendarteritis obliterans. In his opinion, lymphocytic infiltrations are so common in thrombus organization that no conclusion concerning a primary inflammatory lesion can be drawn therefrom.

Jaeger,[9] in two articles based on a thorough necropsy study of four cases and the examination of several surgical specimens, stated that the first change is localized fibrinoid necrosis of the intima. This is followed by proliferation of the cells underlying the necrotic portions,

giving rise to the formation of "intimal cushions." Occlusion may follow this process directly or by way of thrombus formation. The reactive granulation tissue is distinguished by abscesslike leucocytic foci, and later by the presence of Langhans-type giant cells and fibroblasts. The distribution may be extremely widespread throughout the vessels of the viscera and extremities. Consequently, thromboangiitis obliterans is classified by Jaeger as a general inflammatory disease of the vascular system.

Buerger,[10] however, objects strenuously to the above theories regarding the pathogenesis of thromboangiitis obliterans. He states that the essential picture is one of vascular inflammation and occlusive thrombosis, and that degenerative lesions are merely coincidental and bear no causal relation to Buerger's disease. He describes two stages: (1) the acute or specific stage, and (2) the healed or organized stage. In the former the changes consist in an acute inflammatory process characterized by infiltration of the vessel coats with polymorphonuclear leucocytes and the occlusion of the lumen by red clot. The specific lesion is a purulent focus in the clot, containing giant cells, endothelioid cells or "angioblasts," and broken-down leucocytes.

Healing takes place, as far as we can ascertain from Buerger's description, in a manner entirely typical for the organization and canalization of any thrombus. He emphasizes the presence of hemosiderin-filled monocytes in the organizing tissue, but in our experience this is not specific, for it may be encountered in any organizing clot. This process leads finally to the complete obliteration of the lumen of the vessel, with recanalization. He also emphasizes the involvement of the veins, and the perivascular fibrosis which binds together the artery, vein, and nerve.

According to Mallory,[11] however, other investigators, in studying a large volume of material, have found very little evidence of the acute changes described by Buerger. This may be because of the short duration of the acute process, but this point of view denies the necessity of finding acute changes in order to make a diagnosis of thromboangiitis obliterans.

Mallory also states that, in the opinion of some authors, the changes described by Buerger are not specific, but may be found also in the arteries after trauma, in Raynaud's disease, syphilis, ordinary septic thrombophlebitis, and even frostbite.

In the present case the vascular lesions were found in the abdominal aorta, the iliac arteries, the small and medium-sized pulmonary arteries, and the small and medium-sized arteries of the kidneys. Nowhere was an acute inflammatory lesion found. No unorganized thrombi were found except in the iliac arteries, where organization was just beginning. Intimal thickening was found in both occluded and unoccluded vessels. In some portions, particularly in the kidneys, there were splitting and reduplication of the internal elastica. In some of

the canalized thrombi the organizing vessels were definitely muscular in type, and some had a fairly well-formed elastic membrane.

The veins were not involved as far as could be ascertained, nor was the perivascular fibrosis of Buerger's description found.

The lesions in the heart were puzzling in that the arteries were thin-walled and apparently patent, and yet there were large patches of fibrosis that were fairly typical of healed infarcts. In the organizing ventricular thrombi there were hemosiderin-filled monocytes. No importance was attached to this, however, for pigment may be found in any organizing thrombus.

The clinical picture certainly did not correspond to that usually ascribed to thromboangiitis obliterans as manifested in the peripheral arteries. This disease is unusual in women, and especially so in women under 30 years of age. Telford and Stopford[7] concluded from their own cases and those collected from the literature that less than 1 per cent of the total number of cases occurred in women.

In the typical case, the presenting symptoms are pain, numbness, and coldness of the lower extremities, and intermittent claudication. The final result of the vascular lesions is usually gangrene. Besides the symptoms caused by arterial changes, phenomena referable to thrombophlebitis may be striking, and are usually described as being of a migratory nature. Buerger presents thrombophlebitis as an essential feature, whereas Telford and Stopford found it in only 10 per cent of their cases.

In the present case, however, no symptoms referable to the peripheral vessels were noted until the visceral manifestations had been established for several years. This fact, in itself, does not necessarily exclude thromboangiitis obliterans; Hausner and Allen[3, 12] found typical lesions in the visceral arteries preceding those in the peripheral vessels. When our patient finally began to develop the symptoms of peripheral lesions, however, they were not such as would indicate thromboangiitis obliterans. Although she complained of easy fatigue of the legs early in the course of her illness, claudication was never present, nor were there symptoms of migratory thrombophlebitis.

The first indication of involvement of the peripheral vessels appeared about six months before her death. At this time there occurred what seemed to be a major venous occlusion in the left leg. The arterial pulses in this leg disappeared temporarily, but when the edema subsided they reappeared, although they were of small volume.

Again, about two months prior to her death, both legs suddenly became edematous. She complained of heaviness, awkwardness, and numbness of the lower extremities, which now were cold and slightly cyanotic. At this time the arterial pulses disappeared bilaterally, but subsequently reappeared.

The prompt return of the pulses on both of these occasions seemed to rule out the possibility of a major arterial occlusion. The absence

of gangrene bore out this impression, and the finding at autopsy of complete occlusion of both common iliac arteries was totally unexpected.

The nodules on the cheek and left arm, which disappeared before death, remain entirely unexplained. It was considered that these might be related to the vascular system, possibly as a manifestation of periarteritis nodosa, but the vascular lesions which were found in the other organs gave no support to this supposition.

Unfortunately, examination of the brain was not permitted, so that the explanation of the cerebral symptoms must remain entirely a matter of speculation. Hausner and Allen,[3] in discussing the cerebral manifestations of thromboangiitis obliterans, suggested that the transient nature of the symptoms implies a vasospasm superimposed on organic lesions. In their experience, hemiplegia was the outstanding symptom, sometimes accompanied by confusion, disorientation, aphasia, loss of memory, and hemianopsia. A review of twenty-three cases from the literature and eleven cases from the Mayo Clinic by the same authors, in 1940,[12] served to confirm their earlier impressions.

The cause of the cardiac disorder was never thoroughly understood clinically. Although there was a doubtful history of chorea and a definite history of diphtheria in childhood, the cardiac abnormalities were not such as to indicate an infectious origin. Examination of the heart revealed little besides progressive enlargement, persistent tachycardia, and an inconstant apical systolic murmur. The electrocardiogram suggested myocardial damage of a type usually associated with coronary disease. On the other hand, the attacks of pain in the chest were rather typically pulmonary in character, and at no time did they suggest coronary disease. The high diastolic pressure was puzzling, in that there was no indication that the systolic pressure had been elevated previous to the onset of heart failure.

The heart muscle was the seat of patchy fibrosis which is usually considered as the end result of sudden or gradual coronary occlusion. Thorough examination of the vessels, however, revealed no thrombi, and the arteries appeared thin walled and widely patent. It was felt, therefore, that the infarcts must have been caused by prolonged spasm of the arteries. Telford and Stopford[7] stated that the pulses in the affected arteries may come and go; this observation would seem to indicate that spasm may play an important role in the production of the characteristic lesions of thromboangiitis obliterans.

Another possible explanation is suggested by Currens,[13] who, in a recent paper, based on both his own observations and several reports in the literature, called attention to the electrocardiographic changes in cases of pulmonary embolism; he emphasized especially the finding in some of these cases of myocardial infarcts at autopsy, although no coronary occlusion could be detected. He thought that these infarcts were the result of shock and the consequent lowering of the coronary

arterial pressure, combined with an increase in pulmonary arterial tension and an increased demand on the right side of the heart.

The pulmonary lesions could easily have been caused by embolism, thrombosis, or vasospasm, or, indeed, any combination of these. The endocardial thrombi on the right side formed a ready source for emboli. On the other hand, the changes found even in the unoccluded arteries were of a type often associated with vasospasm, which, in turn, may lead to thrombosis. The decrease in blood supply to the lung brought about in this way, with the added factor of a handicapped heart, was probably the cause of the generalized thickening and fibrosis of the lung framework.

The relation between the state of the cardiac function and the acute pulmonary attacks is another subject for speculation. The symptoms which suggested infarction of the lung frequently occurred during a period of improved cardiac status. Since these attacks occurred frequently after the intravenous administration of a mercurial diuretic, it is possible that the vasospasm that was already present might have been aggravated by the drug, precipitating thrombosis. The chief evidence of cardiac improvement was a decrease in the edema, without any slowing of the pulse rate or change in the heart tones. It was felt, therefore, that the improvement was brought about chiefly by the diuretic, and that an increase in the force of cardiac contraction sufficient to dislodge endocardial thrombi did not take place.

The symptoms which we, in retrospect, have attributed to the infarcts of the kidneys were of little specific diagnostic value. Although renal changes were considered as a cause for these symptoms, there was nothing to point to any specific renal lesion. The pain itself was misleading; its location was in the upper abdominal quadrants, and varied not only in successive attacks, but also during a single attack. At no time was there radiation suggesting renal origin. Associated with the pain were fever, nausea, vomiting, distension, and obstinate constipation. The fact that she had had an appendectomy, followed by peritonitis, introduced another confusing factor, i.e., the possibility of intestinal obstruction caused by adhesions.

The urinary abnormalities were not such as to point to the true cause of the abdominal symptoms. The variable albumin content and the presence of casts were felt to be consistent with the cardiac situation. The absence of hematuria merely added to the negative evidence which allowed the abdominal complaints to go unexplained clinically.

In view of the obvious divergence of opinions on the subject, no attempt has been made to put this case in a definite category in the confused classification of vascular occlusive diseases.

SUMMARY AND CONCLUSIONS

1. A case of generalized arterial disease in a young white woman is presented. The vascular lesions involved chiefly the muscular ar-

teries, and consisted of intimal thickening and fibrosis, splitting of the internal elastica, and thrombosis with organization and canalization.

2. The clinical picture was bizarre, and is conceived to have been the result of vascular changes in the brain, heart, lungs, and kidneys.

3. The classification of the condition is considered with reference to the recent literature concerning thromboangiitis obliterans. The opinions of the various authors with regard to the essential nature of this disease, and also with regard to the criteria for its diagnosis, are at variance. It appears either that this disease varies greatly in its manifestations, or that more than one disease is included under this name.

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ELECTROCARDIOGRAPHIC OBSERVATIONS ON 500 UNSELECTED YOUNG ADULTS AT WORK

PHILLIP C. VISCIDI, M.D., AND ARTHUR J. GEIGER, M.D.
NEW HAVEN, CONN.

IN A recent study which involved routine electrocardiographic examination of hospital and dispensary patients,[1] we encountered the surprisingly high incidence of 27.2 per cent of abnormal records among 400 subjects who were selected more or less at random from among patients on whom no formal request for an electrocardiogram had been made. Even after eliminating those cases in which some abnormality might have been expected from the history, blood pressure, physical examination, or laboratory data, an entirely unexpected abnormal group, comprising 12.2 per cent of the electrocardiograms, was still left. Because practically half of the abnormal records were found in the younger age group (13 to 35 years old), and because a higher percentage of unexpectedly abnormal tracings occurred consistently in the earlier as compared with the later decades, it was thought important to extend this study to include a large group of relatively young people who were not patients, but were apparently healthy subjects and at work. The results of such an investigation might be of particular current interest to those concerned with the selection of personnel for highly specialized military and industrial needs, like aviation.

It is necessary to emphasize the importance of basing such a study on subjects who are not *patients,* for illnesses other than those of a primarily cardiovascular nature may nevertheless influence the electrocardiogram. Thus, Sprague[2] has listed forty causes for abnormalities of the RS-T and T portions of the electrocardiogram, only 15 of which are directly concerned with cardiovascular abnormalities, and Leach, Reed, and White,[3] in a recent study of low voltage, found that heart disease was of no greater relative importance than extracardiac factors in cases in which this feature was present.

Should study of a large, nonpatient group again disclose an unusually high incidence of electrocardiographic abnormalities, then at least two considerations would arise: (1) that routine electrocardiography is an essential supplement to other methods of examination and is indispensable as a case-finding method in cardiovascular disease, or (2) that our present criteria of what is normal for the electrocardiogram are faulty.

Representing in part an abridgment and in part an extension of a thesis submitted by P. C. V. to Yale University School of Medicine in partial fulfillment of the requirements for the degree of M.D.

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METHODS AND PROCEDURE

Electrocardiograms were obtained on 500 unselected subjects between the ages of 18 and 38 years. There was an equal number of males and females, and the majority were medical students, nurses, or interns; the remainder were hospital technicians or other institutional employees. A relevant history was recorded on each subject, and all had had or were given at least one complete physical examination, including readings of blood pressure, Kahn test on the blood, and one or more roentgenologic examinations of the chest. All of the subjects were seemingly in good health and at work, at the time of the electrocardiographic examination.

Each electrocardiographic record consisted of the three conventional limb leads, as well as the precordial lead CF_4,[4] and the sensitivity of the galvanometer was adjusted to the standard deflection of one centimeter per millivolt. All records were taken with the subjects in the same semi-reclining position to exclude positional variations.

The amplitudes of deflections were measured to the nearest 0.5 mm., and durations to the nearest 0.01 second. When variations were apparent, an average of several measurements was taken.

The criteria by which the electrocardiograms were judged corresponded almost entirely with the standards found in the current *Nomenclature and Criteria for Diagnosis of Diseases of the Heart*, compiled by the Criteria Committee of the New York Heart Association.[5] These criteria were slightly modified or amplified on the strength of personal experience (indicated by asterisks in the tabulation below) when the authority quoted either made no statement or seemed resting on too little data, as in the case of certain features of Lead CF_4. Although in practice our criteria are slightly broader in certain minor details than those herein referred to, it was felt that, for the purposes of this study, the criteria of a widely used and official authority should properly serve as the basis for judgment.

RESULTS

Classification of the electrocardiograms as normal, borderline, and abnormal, on the basis of the criteria set forth in Table I, revealed that only 244 of the 500 records, or 48.8 per cent, were indisputably normal, while of the remainder the outspokenly abnormal tracings greatly outnumbered those classified as borderline. These results are summarized in Table II.

Before considering the significance of these observations and attempting to interpret them, it was essential first to investigate the subjects with borderline and abnormal electrocardiograms and to ascertain whether there were cardiovascular abnormalities which might account for some of the deviations from the normal. It was found that only fourteen subjects (2.8 per cent) presented either definite or probable cardiovascular abnormalities. Eight had heart murmurs, six of which were considered organic, and two others were accepted as organic, although the description of the murmurs by another examiner had not been adequate and the subjects were no longer available for re-examination. Four persons had roentgenologic abnormalities in the chest. One

TABLE I

CRITERIA OF NORMAL ELECTROCARDIOGRAPHIC FEATURES ADOPTED IN THIS STUDY*
(Amplitudes: 1 mm. = 0.1 mv.)

LIMB LEADS	
P Wave	
Direction:	Upward in Leads I and II (except in dextrocardia)
Amplitude:	0.5 to 2.5 mm. in lead with largest P wave
Duration:	Up to and including 0.10 sec.
Contour:	May be notched if otherwise normal
	†(With respect to the last three, a P wave was judged abnormal only if it exceeded the indicated limits in more than one of the features)
P-R Interval:	0.12 to 0.20 sec.
QRS Complex	
Duration:	Not exceeding 0.10 sec. in lead where longest
Amplitude:	Either 5 mm. or more in at least one lead, †or sum of over-all dimension in three leads more than 15 mm.
Contour:	Notching or splintering or localized slurring in one lead only, or in more than one lead if confined to apex or base in such other leads
	Q waves in Leads I, II, and III not exceeding 15%, 20% and 25%, respectively, of the largest QRS amplitude in any of the three leads (Criteria do not hold if QRS amplitude exceeds 20 mm., or for Leads II and III in presence of right axis deviation)
Axis:	Net deflection is upward or zero in all three leads (†QRS not longer than 0.10 sec.)
RS-T Junction:	Deviation from isoelectric level up to ± 1 mm.
T Wave	
Direction:	†Upward in Leads I and II
Amplitude:	At least 1 mm. in Leads I and II
Q-T Duration:	The value for K in the formula $Q - T = K \sqrt{\text{cycle length}}$ does not exceed 0.392 in men or 0.440 in women
PRECORDIAL LEAD IV F	
P Wave	
Direction:	Upward, isoelectric, †diphasic or †inverted up to -0.5 mm.
Amplitude:	†-0.5 mm. to +1.5 mm.
QRS Complex	
Amplitude:	†Over-all dimension is 8 mm. or more
Contour:	†Slurring, notching, splintering acceptable
	†Initial positive deflection (R wave) not less than 3 mm.
	Initial negative deflection (Q wave) not more than 3 mm.
RS-T Junction:	Deviation from isoelectric level not beyond -0.6 mm. or +2.0 mm.
T Wave	
Direction:	Upright
Amplitude:	0.5 mm. or more

*According to criteria adopted by the American Heart Association.[5]
†Personal modifications or additions to criteria.

TABLE II

CLASSIFICATION OF ELECTROCARDIOGRAMS OF 500 UNSELECTED WORKING SUBJECTS

RECORDS	MALES		FEMALES		TOTAL	
Normal	116	46.4%	128	51.2%	244	48.8%
Borderline	33	13.2%	21	8.4%	54	10.8%
Abnormal	101	40.4%	101	40.4%	202	40.4%

man had hypertension and a past history of auricular fibrillation, and one woman had unexplained, periodic edema of the ankles. The abnormal electrocardiographic and clinical observations in these fourteen cases are summarized in Table III.

TABLE III

CLINICAL AND ELECTROCARDIOGRAPHIC DATA IN THE FOURTEEN PATHOLOGIC CASES ELIMINATED FROM STUDY

ECG NO.	SEX	CLASS *	ECG ABNORMALITIES	CLINICAL ABNORMALITIES
45	M	Ab.	LAD† 1+ (asthenic build) Slurred $QRS_{2, 3, 4}$	Loud systolic murmur and split sound at apex
40	M	B.	RAD‡ ± Slurred $QRS_{2, 3}$ "K" = 0.406	Deformity from previous empyema and thoracotomy on right
63	M	Ab.	Small QRS_4 Slurred $QRS_{1, 2}$	Loud apical systolic murmur. Cardiac displacement (x-ray)
66	M	Ab.	Slurred $QRS_{1, 2}$; Broad P "K" = 0.405	Systolic murmur at apex. Scarlet fever and diphtheria in childhood
97	M	B.	LAD 2+ Slurred $QRS_{1, 2, 3}$	Blood pressure 155/65
236	M	Ab.	LAD 2+; T_2 inverted Slurred $QRS_{2, 3}$	Inconstant hypertension. History of scarlet fever and nephritis
247	M	B.	Slurred $QRS_{1, 2}$ T waves all low	Blood pressure 170/100. Paroxysmal auricular fibrillation
312	F	Ab.	Low QRS_4 with absent R_4	Periodic edema, ? etiology
351	F	N.	LAD 1+	Signs of mitral stenosis
353	F	Ab.	T_2 absent	Harsh apical systolic murmur. Auricular enlargement (x-ray)
360	F	Ab.	Small QRS_4 ($R_4 = 1$ mm.) QRS slurred in all leads	Apical systolic murmur. Patient not available for recheck
415	F	Ab.	Small QRS_4 ($R_4 = 1$ mm.) Low voltage	Left auricular enlargement (x-ray)
447	F	Ab.	QRS slurred in all leads T_2 absent; $S\text{-}T_2 = -2$ mm.	"Systolic murmur" (patient not available for recheck)
452	F	Ab.	T_2 absent, $S\text{-}T_2 = -1.5$ mm.	Blood pressure 140/90

*Ab, Abnormal; B, borderline; N, normal.
†LAD, Left axis deviation.
‡RAD, Right axis deviation.

Elimination of the fourteen abnormal cases from the study still left 242 (49.8 per cent) of the records in the abnormal and borderline groups, of which the great majority were definitely abnormal on the basis of the established criteria. The classification of these records is given in Table IV.

Inspection of Table V reveals that although the abnormal and borderline features consisted predominantly of those in which the personal

element of judgment is necessarily involved (as in slurring of the QRS complex), and others which are not always considered in clinical practice (as with abnormally long Q-T interval), it is to be noted that significant contributions are represented also by features that command every-day attention (such as abnormalities of the T wave, low QRS voltage, and considerable axis shift).

TABLE IV

CLASSIFICATION OF ELECTROCARDIOGRAMS OF 486 APPARENTLY NORMAL SUBJECTS

RECORDS	MALES		FEMALES		TOTAL	
Normal	117	48.2%	127	52.2%	244	50.2%
Borderline	28	11.5%	21	8.6%	49	10.1%
Abnormal	98	40.3%	95	39.2%	193	39.7%

TABLE V

ABNORMAL AND BORDERLINE ELECTROCARDIOGRAPHIC FEATURES ENCOUNTERED IN 500 YOUNG ADULTS AT WORK

ABNORMAL FEATURES	ABNORMAL		BORDERLINE		TOTAL	
	NO.	%	NO.	%	NO.	%
Limb Leads						
P inverted in two leads	1	0.2			1	0.2
P duration exceeding 0.11 sec.	1	0.2			1	0.2
P-R duration of 0.22 sec. or more	4	0.8			4	0.8
QRS duration of 0.12 sec. or more	2	0.4			2	0.4
Low voltage	9	1.8			9	1.8
Slurred in two or three leads	28	5.6	98	19.6	126	25.2
Abnormally deep Q_1	2	0.4			2	0.4
Abnormally deep Q_3	6	1.2			6	1.2
RS-T depressed more than 1 mm.	3	0.6			3	0.6
elevated more than 1 mm.	3	0.6			3	0.6
T abnormal direction or amplitude	21	4.2	1	0.2	22	4.4
Axis shifts more than slight	5	1.0	5	1.0	10	2.0
Frequent ectopic beats			1	0.2	1	0.2
Abnormally long Q-T	85	17.0			85	17.0
Chest Lead IVF						
P inverted 1.0 mm. or more			35	7.0	35	7.0
Q abnormally large	2	0.4			2	0.4
QRS low voltage	78	15.6	2	0.4	80	16.0
R abnormally small or absent	2	0.4	2	0.4	4	0.8
T abnormal direction or amplitude	19	3.8			19	3.8

It is acknowledged that even the most careful selection of normal subjects is not an infallible procedure, but it is unthinkable that practically half of such a large group would have undiscovered causes for electrocardiographic abnormalities. Moreover, this fact recalls our previous disclosure[1] of abnormal electrocardiograms in an unexpectedly high percentage of hospital and dispensary patients who were not afflicted with cardiovascular disease.*

*The higher incidence of abnormalities recorded in the present study, as compared with the earlier one referred to, is probably due largely to two factors: (1) a difference in technique, for many of the electrocardiograms in the previous investigation were visualized on a fluoroscopic lag-screen attachment to the electrocardiograph, and some abnormalities might have escaped detection, and (2) no attention was paid in the previous study to Q-T duration, which directly contributed twenty-nine records to the abnormal group.

The conclusion seems forced that the current criteria of normality for the electrocardiogram are faulty in being too narrow, and, on the basis of such criteria, we agree with the recent observations of Wood, Wolferth, and Miller[6] that electrocardiographic surveys would be misleading if applied as a screening technique in mass examinations of candidates for specialized military and industrial posts, or in examinations of life insurance applicants.

SUMMARY AND CONCLUSIONS

An electrocardiographic study of 500 apparently healthy, young, working adults disclosed that half of the records fell outside the range of normal on the basis of authoritative electrocardiographic criteria of normality in current general use. The implication is that electrocardiographic surveys will be misleading unless criteria of what is normal are revised and broadened.

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ON CERTAIN APPLICATIONS OF MODERN ELECTROCARDIOGRAPHIC THEORY TO THE INTERPRETATION OF ELECTROCARDIOGRAMS WHICH INDICATE MYOCARDIAL DISEASE

ROBERT H. BAYLEY, M.D.
NEW ORLEANS, LA.

INTRODUCTORY REMARKS

FOR nearly thirty years the medical profession has been interested in the problem of interpretation of the electrical effects of the heartbeat. The property of living cells which is characterized by their ability to produce detectable electrical effects is called excitability. This is a property enjoyed not only by cardiac muscle, but by nerve and striated muscle as well. A striking similarity exists between the electrical effects of excitability in these different kinds of tissues and in other cells of both the plant and animal kingdoms. The fields are new and in them much awaits to be done.

An understanding of the electrical effects produced by the heartbeat is not easily obtained by the physician. The chief difficulty lies in the fact that men who are trained primarily as physicians must herein deal with the relatively foreign agent, electricity. Physicists have found that electricity is most conveniently described in mathematical language, but mathematics is a tool for which most physicians entertain a strong aversion. Consequently, a treatise of this kind, although it demands an occasional mathematical expression for accuracy's sake, is best supported by word pictures as well. The more advanced mathematical expressions, which are not essential for a useful grasp of the subject, are relegated to footnotes. Expressions which are retained in the main body of the script are of a simple kind and lend themselves to direct geometric visualization. It is all too obvious that only those physicians who have undertaken the laborious task of becoming familiar with the relevant theoretical physics of electricity are in a position to formulate sound electrocardiographic theory. Between past and present investigators, who are thus qualified, there have been and are no important differences of opinion regarding the interpretations placed upon their own investigative observations or those of others.

From the Department of Medicine of the School of Medicine of Louisiana State University.
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SECTION I

ON VECTORS AND ELECTRICITY

One may choose any number and give it a sense, positive or negative. The number is now a scalar quantity with two properties, magnitude and sense. Certain quantities are met with in dealing with electricity which possess direction as well as magnitude and sense. These are referred to as vector quantities. They are defined completely by the directed line or vector. The direction of the line, indicated by the arrowhead, is the direction of the vector. The length of the line denotes the magnitude of the vector. The sense of the vector is indicated by the plus (usually omitted) or minus sign. The point in space from which the directed line begins is called the origin of the vector. The point in space at which the directed line ends is called the terminus of the vector. In script, vectors or the quantities which they represent are denoted by boldface or clarendon type or by an arrowhead over the letter.

The present subject demands familiarity with three manipulations of vectors, i.e., the translation of a vector, the sum of two or more vectors, and the projection of a vector.

Any two vectors are considered equal if they are identical in direction, magnitude, and sense. The translation of a vector is performed by moving the vector about in space from one position to another without changing its direction, magnitude, or sense. A vector is obviously equal to each of its translations. When the sense of a vector is altered from negative to positive, or vice versa, its direction in space is reversed.

In forming the sum of two vectors $\hat{A}$ and $\hat{B}$, a translation of the vectors to a common origin is first carried out. The parallelogram of which $\hat{A}$ and $\hat{B}$ form two sides is then completed. Finally, a directed diagonal of the parallelogram is drawn, commencing at the common origin of the two vectors. The directed diagonal $\hat{C}$ is a new vector representing the sum or resultant of the vectors $\hat{A}$ and $\hat{B}$. Thus, the meaning of the relation,

(1-1) ... $$\hat{A} + \hat{B} = \hat{B} + \hat{A} = \hat{C},$$

is made clear. An angle formed by two vectors, such as that formed by $\hat{A}$ and $\hat{B}$ before or after translation, may be denoted by the symbol $(\hat{A},\hat{B})$. The occasion often arises in which it is desired to refer to the magnitude of a vector rather than to the vector itself. For this purpose the notation usually adopted is that which uses the corresponding capital letter uncovered by the arrowhead. Thus A is the magnitude of the vector $\hat{A}$. Moreover, if the magnitude of the vector $\hat{A}$ is 10 units, we have the following identities, $\hat{A} = A\hat{a} = 10\hat{a}$, and $A = 10$. The first three equalities are vector expressions, whereas the last two are scalars. A vector quantity is never equated to a scalar quantity.

In order to project a vector upon a line or plane, two normals are dropped from the extremities of the vector upon the line or plane. The

directed line connecting the feet of the normals is a new vector, the projection of the former upon the line or plane. One normal always connects the origins of the two vectors and the other connects their termini. Let $\hat{A}$ be a vector and let $\hat{B}$ represent the projection of $\hat{A}$, then[1]

$$\hat{B} = A \cos(\hat{A},\hat{B})\ \hat{b}, \qquad (1\text{-}2)\ \ldots$$

where $\hat{b}$ is a unit vector in the direction of $\hat{B}$, and the quantity $A \cos(\hat{A},\hat{B})$ is a scalar representing the magnitude of $\hat{B}$ in terms of the magnitude of $\hat{A}$ and the angle made by the vectors $\hat{A}$ and $\hat{B}$. The validity of eqn(1-2) is made obvious in the following way. Let $\hat{B}$ (Fig. 1, *a*) be the projection of $\hat{A}$ upon the line op. In the right triangle, cos $(\hat{A},\hat{B})$ is by definition B/A. Consequently,

$$B = A \cos(\hat{A},\hat{B})$$

and

$$B\hat{b} = A \cos(\hat{A},\hat{B})\hat{b}$$

so that

$$\hat{B} = A \cos(\hat{A},\hat{B})\hat{b}$$

which states that the projection of a vector (upon a line or plane) is itself a vector with a magnitude equal to the product of the magnitude of the projected vector by the cosine of the angle made by it and its projection, and having the direction of the projection.

We may regard electricity as consisting of minute particles, called electrons, which have mass and possess a negative charge. The nature of the electricity with which we are at present concerned is the so-called ionic electron charge. When molecules of certain substances are in solution they dissociate to a variable extent into particles of one or more elements, called ions, which possess either a positive or negative charge. The positively charged ion is known as the cation, and the negatively charged ion is known as the anion. Between any two ions of unlike charge, or between any two groups of ions of unlike charge, there exists a force of attraction. The force acts in accordance with a fundamental law of electricity which states that unlike charges attract, and like charges repel, each other.

The ability of an electric source to produce a flow of current in the region surrounding the source is another electrical fundamental. Every point in the region surrounding an electric source at which the flow of current is present constitutes the electric field due to the source. The medium in which the source is located and throughout which the field extends is known as the *conductor*. When a positive source distribution is responsible for an electric field, the source distribution is referred to as the source of the field. When a negative source distribution is responsible for a field, the former is referred to as the sink of the field.

It is clear that, if the bio-electric process under consideration is in the nature of an electrolytic dissociation, the field will be produced by both sources (+ ionic charges) and sinks (– ionic charges). The particular spacial arrangement of the sources and sinks is called the source-sink distribution. If the medium which surrounds the distribution extends in all directions, it constitutes a volume conductor. If each part of the volume conductor is composed of a like substance, or substances which conduct alike, the medium is said to be homogeneous.

In man we are dealing with a source-sink distribution within the heart muscle which generates an electric field extending outward in all directions to the body surface. Although the body trunk is composed of different kinds of tissues, and is not, therefore, homogeneous, the concentration of electrolytes in the various regions is sufficiently similar to permit treating the body as a homogeneous volume conductor.[2] Inasmuch as the body is surrounded by air, a nonconducting medium, the electric field produced by the heartbeat does not extend beyond the body surface.

The distribution of current flow throughout the field in a volume conductor of this kind depends upon the particular distribution and strength of the source-sink combination, upon the extent and shape of the conductor, and upon the particular composition of the conductor.

Perhaps the most simple example is the field produced by a point source in a homogeneous volume conductor of infinite extent. The direction of the flow is radially outward from the source in all directions along straight lines extending from the source to infinity. Let us consider any point p in the field. The electrical force at p is a vector quantity with the properties of direction, magnitude, and sense, and is referred to as the electrical intensity at p. The direction of the electrical intensity along a line (of force) in the field determines the direction of the current flow. The line of force is thus referred to as the line of flow. If the vector $\hat{E}$ denotes the electrical intensity at p, then, by the usual notation, the magnitude of the intensity is E. If e denotes the strength of the point source, and r denotes the distance of p from the source, it is known that

$$(1\text{-}3)\ldots \qquad E = \frac{e}{r^2},$$

which states that the magnitude of the electrical intensity at any point in the field is directly proportional to the strength of the source and inversely proportional to the square of the distance of the field point from the source. Moreover, if $\hat{e}$ is a unit vector in the direction of $\hat{E}$, we may write

$$(1\text{-}3)\ldots \qquad \hat{E} = \frac{e}{r^2}\hat{e}.$$

Another important property of the electrical field is the so-called electrical potential. Let us imagine that we have access to a minute positive "test particle" of negligible mass which we can carry about and place at any arbitrary field point. The charge on the particle is regarded as too small to have any effect on the field, that is, too small to be regarded as part of the source of the field. If the particle is carried to any field point p, it will be acted upon by the electrical intensity at p.

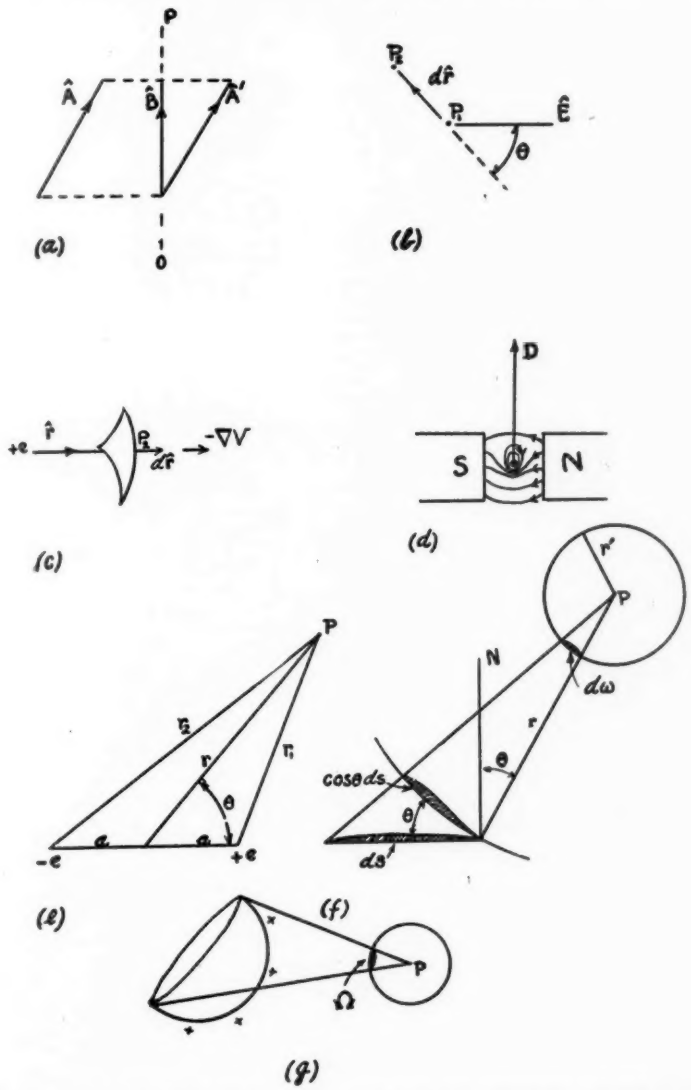

Fig. 1.—(*a*) The projection of a vector. (*b*) and (*c*) Geometry for the calculation of the potential. (*d*) Galvanometer string movement. D indicates the direction of displacement when the current flows into the paper. (*e*) Doublet potential. (*f*) Geometry of the solid angle. (*g*) Visualization of the solid angle subtended by the closed boundary of an arbitrary double-layer surface at the field point p. See text.

Inasmuch as the sense of the source and the sense of the particle are both positive, the action is one of repulsion. If the test particle is released at p, the force of repulsion will carry the particle in a direction away from the source to some point outside the field, that is, to infinity. If we start from infinity, and carry the particle to any field point p, work is done in overcoming the force of repulsion. The amount of work done may be regarded as stored up on the particle in the form of energy of position which may be reclaimed in the form of energy of motion when the particle is released and returns to infinity. While the particle is at p, its energy of position is equivalent to the so-called electrical potential at p. Consequently, we may define the electrical potential at any point in the field as numerically equal to the work done in carrying a test particle from outside of the field to the point in question. When the field is due to a point sink, the action on the particle is one of attraction, and the work done is then regarded as a negative quantity. The electrical potential is thus a scalar quantity. Its value in our present example may readily be found.*

The resistance of a conductor may be defined as the property which enables it to offer a measure of difficulty to the flow of electricity through it. The amount of resistance offered by a given conductor depends,

*Let the potential V_1 at the field point p_1 (Fig. 1, *b*) be less than the potential V_2 at the field point p_2. Let $d\hat{r}$ denote the element of path in the direction of the displacement p_1p_2. The increase of potential dV encountered in traversing the displacement in the direction of $d\hat{r}$ is numerically equal to the amount of work done in carrying a test particle from p_1 to p_2 against the force of repulsion, or the electric intensity $\hat{E}$. Let θ denote the angle $(\hat{E}, d\hat{r})$. Then $E\cos\theta$ is the magnitude of the intensity encountered in traversing the displacement $d\hat{r}$. The product of this force by the dis.ance dr is equivalent to the amount of work done in carrying the test particle over the path p_1p_2. That is,

$$dV = E\cos\theta\ dr = \hat{E} \cdot d\hat{r}$$

But the electric intensity $\hat{E}$ is equal to the negative gradient of scalar potential $-\nabla V$. Also, at any distance r from e, $\hat{E} = \frac{e}{r^3}\hat{r}$ (by Coulomb's law). Thus we have (see Fig. 1, *c*)

$$dV = -\nabla V \cdot d\hat{r} = -\frac{e}{r^3}\hat{r} \cdot d\hat{r} = -\frac{e\,dr}{r^2}$$

Let us denote by R the distance from e to the field point p_2. Then, the potential at p_2 is equivalent to the amount of work done in carrying the test particle from infinity to p_2 by any path. That is

$$V = -e\int_{\infty}^{R} \frac{1}{r^2}\ dr$$

When computing the integration we may use the standard formula $\int X^n\,dx = X^{n+1}/n+1$, where $X = r$, and $n = -2$. Thus

$$-e\int_{\infty}^{R} \frac{1}{r^2}\ dr = -e\left(-\frac{1}{r}\right)_{\infty}^{R} = -e\left[\left(-\frac{1}{R}\right) - \underset{r\to\infty}{\text{Lim}}\left(-\frac{1}{r}\right)\right],$$

where the limit approached by $-\frac{1}{r}$ as $r \to \infty$ is zero. Consequently,[3]

(1-4) . . . $$V = \frac{e}{R}$$

This expression indicates that the potential is directly proportional to the strength of the source and inversely proportional to the distance from the source to the field point at which the potential is measured.

among other things, upon the particular kind of material of which the conductor is composed. The specific resistance of a conductor may be defined as the amount of resistance offered by a cubic centimeter of the substance to the flow of current through it. If we denote by k the value of the specific resistance, its reciprocal 1/k is known as the specific conductivity of the conductor. The value of the potential has been found to vary inversely with k. In our example, the potential V varies directly with the strength of the source and inversely with the distance of the field point from the source. Hence,

$$(1\text{-}5)\ldots \qquad V = \frac{1}{k}\frac{e}{r}.$$

An electrical field may conveniently be regarded as made up of lines of flow and equipotential surfaces. A line of flow is defined as a line drawn in an electrical field in such a way that its direction at every point has the direction of the electrical intensity at that point. All lines of flow begin on sources and terminate on sinks. In our example of the point source in an infinite homogeneous volume conductor, the lines of flow commence at the source and extend outward in all directions along straight courses to terminate upon a sink "scattered at infinity."

Thus far, the more important properties of an electrical field produced by a most simple source distribution have been briefly discussed. It is observed that the relations connecting certain of these properties are likewise quite simple. Since the electrical field depends upon all the sources and all the sinks, as well as upon the size and shape of the conductor, the relations connecting the properties of the field will, in general, become more complex when the source-sink distribution is more elaborate or when the extent of the conductor is finite and of asymmetrical form.

Actually, the value of the potential at a field point cannot be measured conveniently. The instrument used is a galvanometer which must be connected with the field at two points by lead wires from its two terminals. An electric current then flows through the galvanometer from the field point at which the value of the potential is great, and enters the conductor at the field point at which the value of the potential is relatively small. The strength of the current flowing through the galvanometer is proportional to the difference of the values of the potential at the field points under investigation. For this reason the galvanometer is said to measure the potential difference (P.D.) across the two field points in question. The P.D. is commonly referred to as the measured electromotive force (E.M.F.). If V_1 and V_2 denote the great and small values, respectively, of the potential at the field points, we have

$$(1\text{-}6)\ldots \qquad \text{E.M.F.} = V_1 - V_2.$$

The current, in completing the body-galvanometer circuit, flows from one field point to the other through the galvanometer and back

to the point of high potential through the conductor of the field. The measured E.M.F. may, therefore, be looked upon as a vector quantity with a magnitude which is determined numerically by the value of the P.D., a direction away from the point of low toward the point of high potential, and always a positive sense.

The instrument in general use is the string galvanometer of the Einthoven type. Its essential parts consist of a horseshoe-shaped field magnet with its north pole N and south pole S (Fig. 1, *d*) opposing each other across a small gap. From the north pole N to the south pole S are straight parallel lines of magnetic force which comprise the effective magnetic field. Piercing the magnetic field at right angles to the lines of magnetic force is a delicate fiber (a quartz thread coated with gold or silver) which conducts the current that is led off the electrical field under investigation. When this current flows through the galvanometer fiber, it creates an electromagnetic field about the fiber. The character of this field may be determined by the right hand rule, i.e., imagine the fiber grasped with the right hand in such a way that the thumb rests along the fiber in the direction of the current flow; the direction of the circular lines of electromagnetic force is then given by the direction of the fingers grasping the fiber.

Let us consider the gap where the field produced by the current in the fiber is impressed upon the field of the magnet. On one side of the fiber the directions of force of both fields are alike. On the other side of the fiber their directions are unlike. Consequently, the total strength of the two fields is greater on the former than on the latter side, and the fiber will move away from the strong, toward the weak, field. The displacement of the fiber is proportional to the strength of the current flowing within it, and the direction of the displacement is according to the direction of the current flow. If the index finger of the right hand is held straight, and this finger and the thumb and middle finger are held in mutually perpendicular directions, and if the hand is now turned in such a way as to make the index finger point in the direction of the current flow within the fiber while the middle finger points in the direction of the lines of magnetic force of the field magnet, the direction of the thumb indicates the direction of the displacement of the fiber (Fig. 1, *d*). A source of light is used to cast the shadow of a small segment of the fiber upon a moving sensitive film. The motion of the film, together with the motion of the fiber, serves to graph the completed record. The motion of the film is at right angles to the line of displacement of the fiber. Consequently, time is the independent, and voltage the dependent, variable. Whether a given electrocardiographic deflection is positive (above the base line of the curve) or negative (below the base line of the curve) will depend simply upon the direction of the current flow within the fiber or upon the relative values of the potential at the two field points under investigation.

SECTION II

ON THE ELECTRICAL EFFECTS PRODUCED BY THE CARDIAC MUSCLE CELL

Inasmuch as the electrical effects produced by a mass of cardiac muscle represent the sum of the effects produced by the muscle cells individually, a discussion of the latter, more simple, mechanism serves doubly well for introduction.

It is convenient to assume that the cardiac muscle cell is of cylindrical form. Actually its form is, for our present purpose, immaterial. Presumably a protoplasmic layer bounds the cytoplasm and acts during certain periods as a semipermeable membrane with respect to the electrolytic content of the cytoplasm. A membrane of this kind permits cations to diffuse through it while it holds the anions back. Diffusion continues until the electrostatic force exerted between the ions on the two sides of the membrane is equal to the force of diffusion or osmotic pressure. Thus a state of equilibrium is reached, and the cell is said to be in the resting electrical state. The positive charge on the cations outside the membrane and the negative charge on the anions inside the membrane serve as the source and sink distribution for the production of an electrical field. The layer of sources on the outer surface, considered together with the layer of sinks on the inner surface, is spoken of collectively as a double-layer. The magnitude of the source per unit of membrane surface is equal to the magnitude of sink per unit of membrane surface. The magnitude or strength of the source-sink distribution per unit of membrane surface is the same for all parts of the membrane, and the cell is said to be polarized. The term "intensity of polarization" refers to the strength or electrical moment of double-layer per unit of membrane.[2]

The relation* $V = \phi\,\Omega$ is very useful in electrocardiographic analysis,

*It is desirable to know the nature of the electrical field produced by the resting cell. The double-layer has the configuration of a closed cylindrical surface, and the cell is regarded as lying within a homogeneous conducting medium of large extent. The double-layer is regarded as composed of point sources and point sinks. Neglecting the nature of the substance of which the conductor is composed, the potential V_1 at any point p due to a point source is given by eqn (1-4); that is,

(2-1) . . . $$V_1 = \frac{e}{r_1}$$

and in a similar manner the potential V_2 at p due to a point sink is given by the relation

(2-2) . . . $$V_2 = -\frac{e}{r_2}$$

where e and $-e$ of these relations represent the strengths of the source and sink, respectively, and where r_1 and r_2 are the respective distances from the source and from the sink to the field point p. The potential V at p due to both source and sink is given by the sum of the right-hand members of eqns (2-1) and (2-2); that is

(2-3) . . . $$V = e\left(\frac{1}{r_1} - \frac{1}{r_2}\right)$$

Upon writing the fractions with a common denominator and multiplying the numerator and the denominator by $r_2 + r_1$, we have

(2-4) . . . $$V = e\left(\frac{r_2^2 - r_1^2}{r_1 r_2 [r_2 + r_1]}\right)$$

(Footnote continued on next page.)

and its application is reasonably simple. V denotes the potential at a point in the field produced by an arbitrary area of double-layer. The numerical value of the constant ϕ is not known at this time, and is, in fact, immaterial for our present purpose. Actually, ϕ has the dimensions of an electromotive force across the double-layer, and its value depends upon a number of factors.[2] On the other hand, the solid angle is shown in Fig. 1, *g*, and appears subtended at an arbitrary field point p by the boundary of an arbitrary section of double-layer. The solid angle Ω is defined and measured by the area of spherical surface cut off the unit sphere (inscribed about p) by the cone formed by drawing lines from p to every point upon the boundary of the double-layer. The sense of the solid angle is positive or negative, according to whether an observer stationed at p, and looking through the base of the cone, views the positive or negative charge on the double-layer. During this operation the membrane is conveniently regarded as opaque. In practical application, it is not necessary to calculate the area cut off the unit

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Let us consider Fig. 1, *e*. The cosine law states that, for any triangle, the square of the side opposite an angle is equal to the sum of the squares of the other two sides, less twice the product of these sides by the cosine of their included angle. Moreover, the supplementary obtuse angle is $180° - \theta$; thus, $\cos(180° - \theta) = -\cos\theta$. We may now express r_2 and r_1 in terms of r, a, and θ. We get $r_2^2 = r^2 + a^2 + 2ar\cos\theta$, and $r_1^2 = r^2 + a^2 - 2ar\cos\theta$. Consequently, $r_2^2 - r_1^2 = 4ar\cos\theta$. Inserting the right-hand member of the last relation for its identity in eqn(2-4), we have

$$(2\text{-}5)\ \ldots \qquad V = e\frac{4ar\cos\theta}{r_1r_2(r_2 + r_1)}$$

Inasmuch as the source and sink lie very close together, a is very small in comparison with r, so that r_1 and r_2 become nearly equal to r. Here, the source-sink distribution is known as a doublet, and the denominator of the fraction in eqn(2-5) is equivalent to $2r^3$. Thus[2]

$$(2\text{-}6)\ \ldots \qquad V = 2ae\frac{\cos\theta}{r^2}$$

If we denote the constant 2ae by ϕ, the latter is known as the moment of the doublet, and the right-hand member of eqn(2-6) becomes $\phi\cos\theta/r^2$.

The double-layer under consideration may be regarded as composed of a sheet of doublets arranged to form an arbitrary curved surface S, in which the axis of each doublet is in the direction of the outward drawn normal to S. The elementary potential dV at p, due to an element ds of surface S, may be written down at once from eqn(2-6). Thus,

$$(2\text{-}7)\ \ldots \qquad dV = \phi\frac{\cos\theta}{r^2}\,ds,$$

where r is the distance from ds to p; N (Fig. 1, *f*) is the outward drawn normal to S; θ is the angle made by N and r; and ϕ, a constant, is the electrical moment of the double-layer. Let a sphere of radius r be inscribed about p. The angle made by ds and the small portion of the spherical surface adjacent to ds is equivalent to θ, for the corresponding sides of these angles are mutually perpendicular. Inasmuch as ds is an infinitesimal, $\cos\theta\ ds$ is merely the projection of ds upon the spherical surface of radius r.

Let a spherical surface of radius $r' =$ unity be inscribed about p, and let lines be drawn from p to every point upon the boundary of ds. The cone thus formed cuts an area of spherical surface $d\omega$ from the unit sphere, and an area of spherical surface $\cos\theta\ ds$ from the sphere of radius r. Moreover, $d\omega$ is defined as the elementary solid angle subtended at p by the boundary of ds. Obviously, $\cos\theta\ ds/r^2 = d\omega/r'^2$, for both $\cos\theta\ ds$ and $d\omega$ are areas of spherical surface cut off from concentric spheres by the same cone. In this last equality, however, r'^2 is simply unity. Hence, $\cos\theta\ ds/r^2 = d\omega$. Consequently, $dV = \phi\ d\omega$, which, on integration, becomes[3]

$$(2\text{-}8)\ \ldots \qquad V = \phi\iint_S d\omega = \phi\Omega$$

The surface integral expresses the sum of all the elementary solid angles subtended by the surface elements of S at p. Hence, Ω is the solid angle defined and measured by the area cut from the unit sphere by the cone formed by drawing lines from p to every point upon the boundary of the double-layer S.

sphere by the cone. On the contrary, it is sufficient to simply visualize geometrically the magnitude and sense of the solid angle. Inspection of Fig. 1, *g* shows at once that the magnitude of the solid angle is entirely independent of the configuration of surface of double-layer.

It will be instructive to examine further the potential of the field produced by the arbitrary hemispherical distribution (Fig. 1, *g*) of double-layer. If the field point lies anywhere in the plane circumscribed by the boundary of the double-layer, the cone degenerates into this plane surface and cuts off half of the surface of the unit sphere inscribed about the new field point in question. The whole surface of the unit sphere is 4π. Hence, the magnitude of Ω is 2π for all points in the plane specified. If the field point is anywhere in the extension of this plane beyond the boundary of the double-layer, the cone again degenerates into a plane surface, but cuts no area off the unit sphere. Consequently, Ω is zero and the potential at any such point is zero. Finally, if the field point is anywhere upon the axis normal to, and intersecting, the center of the plane circumscribed by the boundary of the double-layer, Ω is numerically maximum with respect to its value at all other points not on the axis at a like distance from the intersection.

Let us now choose any field point p_1 inside the closed surface of double-layer of the resting cylindrical cell. Let any plane whatever be passed through p_1, thus dividing the closed surface of double-layer into two parts. The magnitude of Ω at p_1, due to one part of the double-layer, is 2π and negative. The magnitude of Ω at p_1, due to the other part of double-layer, is likewise 2π and negative. Hence the potential at any point p_1, inside the resting cells, is $-4\pi\phi$, and this value holds for a resting cell of any shape whatever.

Let us denote by p_2 any field point outside the double-layer of the resting cell. We may let any plane whatever pass through the closed surface of double-layer, thus dividing it into two parts. The solid angle subtended at p_2 by the boundary of one part of the double-layer is equal in magnitude and opposite in sign to the solid angle subtended at p_2 by the boundary of the other part of the double-layer. Hence the potential at any point outside the closed surface of double-layer is zero. Moreover, the potential difference encountered while traversing the double-layer is $4\pi\phi$.

The foregoing relations are based on the assumption that the extent of the conductor is infinite. They must hold for practical purposes, however, in defining the potential of the field near by a double-layer situated at the center of an extensive homogeneous volume conductor.

When the resting cell is stimulated, a change in the characteristics of the membrane takes place at the point of stimulation and spreads with a uniform velocity in all directions throughout successive elements of membrane. The first event in the change of membrane characteristics is such that the polarity of the source-sink distribution is reversed.[4] The

term accession has become attached to the initial reversal of polarity. The apparent movement of the reversal process along successive elements of membrane is referred to as the accession wave. When the polarity of the double-layer has become reversed at all points, the cell is said to be in the active or excited electrical state. In a relatively brief time after accession, a second wavelike change of membrane characteristics takes

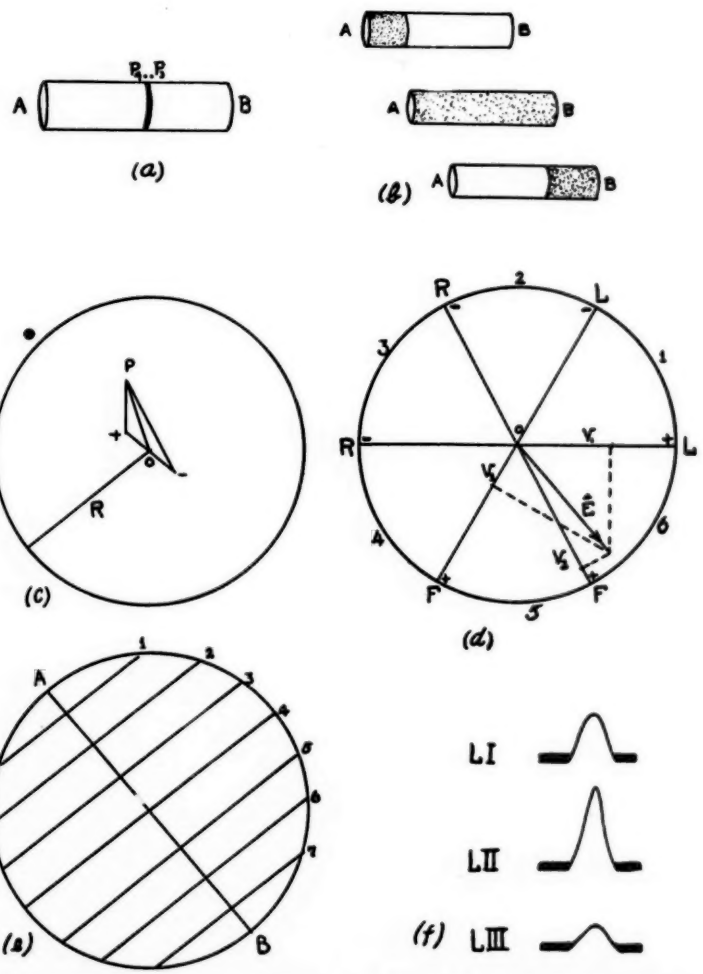


Fig. 2.—(*a*) The visualized boundary of the accession wave moving along the cell AB in the direction of B. (*b*) The nose of the regression wave appearing first at the stimulated end A of the cell (upper diagram), and reaching the end B ahead of the appearance of the tail at A (middle diagram). The lower diagrams shows the tail of the regression wave reaching the end B. (*c*) Showing a spherical conductor of radius R with a doublet at its center. (*d*) The triaxial reference system with the instantaneous electrical axis $\hat{E}$ translated to the origin O. V_1, V_2, and V_3 are the projections of $\hat{E}$ upon the reference axes RL, RF, and LF. (*e*) A spherical mass of cardiac muscle stimulated at the point A. The numbered lines illustrate successive boundaries of the accession wave during its spread in the direction of B. Boundary 4 is a great circle, at which time the potentials (shown in the neighboring diagram) are maximum. (*f*) The accession potential differences produced by stimulation of the muscle mass shown in (*e*). See text.

place. Essentially, the change consists of a second reversal of polarity and is referred to as regression. The apparent movement of the second reversal over the cell is called the regression wave. The rate of regression at a point (or of a single element of membrane) is much slower than the rate of accession at a point. The velocities of the two waves, accession and regression, tend to be like and uniform.

In the region of the cell where accession is in progress (Fig. 2, *a*), a succession of interfaces cuts the membrane at right angles, one interface for each phase of polarity reversal. If the rate of reversal at a point is sufficiently rapid, so that the length p_3p_4 of accession is practically instantaneous, we may let ϕ_1 and ϕ_2 denote the respective moments of the resting and the excited double-layers.* Consequently, the accession potential is directly proportional to the constant given by the sum of ϕ_1 and ϕ_2.

*From eqn(2-8) we get for the accession potential V_a

(2-9) . . . $$V_a = (\phi_1 + \phi_2) \iint_S d\omega = (\phi_1 + \phi_2)\, \Omega$$

where ϕ_1 and ϕ_2 are the respective moments of the resting and the excited double-layers, and where Ω is the solid angle subtended twice (at the field point at which V_a is measured) by the boundary of the resting and the excited double-layers. Outside the cell the magnitude and the sense of Ω are the same, respectively, with each subtending, whereas they differ respectively with each of the two subtendings at an inside point. In the particular case where $\phi_1 = \phi_2$, V_a at any outside point is given by $2\phi_1\Omega$, and at any inside point in the plane of the wave, V_a is zero. In the particular case where $\phi_2 = \phi_1/2$, V_a at any outside point is $3\phi_1\Omega/2$, and at any inside point in the plane of the wave $V_a = -\pi\phi_1$.

In general, the variety of surface over which the integral of eqn(2-9) is taken will be one of three kinds, a first, a second, and a third. A surface of the first kind is defined as closed, and the integral vanishes, so that V_a is zero. A surface of the second kind is defined as bounded by one closed curve situated at the epicardial or the endocardial surface of the ventricles, and it is by this closed curve that the solid angle is subtended. A surface of the third kind is defined as bounded by two or more closed curves, and V_a is given proportionally by the sum of two or more solid angles reckoned with their proper sense and subtended by whatever number of closed curves are formed upon the ventricular surfaces.

The regression potential V_r at any point outside the lamellar source-sink distribution is given by[5]

(2-10) . . . $$V_r = \iint_S (\phi_3 + \phi_4)\, \frac{\cos\theta}{r^2}\, ds$$

where ϕ_3 and ϕ_4 are the respective moments of the resting and the excited types of double-layer; r is the distance from the surface element ds to the field point at which V_r is measured; and θ is the angle made by r and the outward drawn normal to ds. In general, the values of the moments differ both with respect to one another and with respect to one lamella as compared with another. At any given instant during regression, the source-sink distribution is composed of lamellae of the first, second, and third kind, singly or in combination. If all lamellae are of the first kind, the integral vanishes and V_r is zero. The boundary of lamellae of the second kind and the boundaries of lamellae of the third kind are all closed curves upon the endocardial and epicardial surfaces of the ventricles. The regression potential, except for a proportional factor, is given by the sum of the solid angles subtended by the aggregation of closed curves. The potential of a zone of injury or ischemia is likewise dependent upon an aggregation of closed curves constructed upon the ventricular surfaces (Fig. 9).

Evidently, the important conclusion follows that the accession potential, the regression potential, and the injury potential depend only upon the activity of the muscle units at the ventricular surfaces, and are independent of the activity of the muscle units between these surfaces. In the case of local muscle death, the residual living muscle possesses a new and abnormal surface adjacent to the dead region, a surface at which certain of the closed curves must lie. The general conclusion which states that the normal or abnormal electrocardiogram may be reckoned from an aggregation of closed curves constructed upon the muscle surfaces is further supported by the well-known physical fact that the field strength $\mathfrak{E}$ at any field point outside a distribution of the kind herein considered may be expressed not only by the negative gradient of scalar potential, but also by the sum of a number of vectors, each of which is given by the curl of the curve-potential of a closed curve multiplied by the respective moment.[6]

If the accession wave, having commenced at A, reaches B before regression begins, the excited double-layer is closed. Thus, everywhere outside the excited cell the potential is zero, and, everywhere inside, the potential is $4\pi\phi_2$.

Fig. 2, *b* illustrates the situation encountered during regression. In the upper diagram, regression has commenced at the end, A, of the cell, and the front of the regression wave is advancing in the direction of B. The second reversal of polarization is occurring throughout the shaded region. In the center diagram, the front of the wave has reached B before the tail of the wave appears at A. Here, the length of the regression wave exceeds the length of the course over which the wave appears to pass. Consequently, the whole surface of the cell is in the process of reversing its membrane polarity. In the lower diagram, the tail of the regression process is seen advancing in the direction of B. Throughout the unshaded regions, the subdivision of the cell is in the excited state (upper diagram) and in the resting state (lower diagram).

Throughout the shaded regions of the diagrams, it may be regarded that there is a succession of double-layer boundaries in pairs. The two double-layers associated with any one pair of boundaries differ in that their polarities with respect to the two sides of their membranes are unlike. They likewise differ in the configuration of their surfaces, i.e., one is concave toward A and the other is concave toward B. Each pair of boundaries defines a lamina of source-sink distribution which defines the local subtotal change of polarization. The total distribution is said to be lamellar. The electrical moments of the various laminae differ, inasmuch as the rate of regression at a point is not constant.* The regression potential is, therefore, a function of the rate of regression at a point.

The deflections on the completed record produced by regression are called the regression deflections, whereas those produced by accession are called the accession deflections.

The foregoing considerations make it clear that a cell in the resting or in the excited electrical state produces no outward electrical manifestations. Consequently, all of the normal electrical manifestations of the heartbeat occur while the heart's cells are in the process of passing from the resting into the excited state, and again while the cells are in the process of passing back from the excited into the resting state.

Because of more or less obvious technical difficulties, the electrical effects of a single cardiac muscle cell cannot be recorded. A mass of cardiac muscle immersed in an extensive homogeneous conducting medium acts, however, in a manner altogether similar to that described for the single cell.[5] As the accession wave spreads from one cell to another in a direction everywhere away from the point of stimulation,

*See footnote page 781.

the effective boundaries of the double-layers move, or appear to move, along the limiting surface of the muscle mass, and the solid angle subtended by them is equivalent to the sum of all the solid angles subtended by the many boundaries of all the double-layers of all the cells which are involved by the accession process at the instant considered.

For the purpose of recording the potential at a point, one electrode, the exploring, is placed at a point in the conductor near the muscle under investigation, whereas the other electrode, the indifferent, is placed at a relatively remote point at or near the surface of the conductor. Under the circumstances, the potential at the indifferent electrode is relatively small in comparison with simultaneous values of the potential at the exploring electrode. Consequently, the effects on the completed record may be regarded as characteristic of the potential fluctuations at the exploring electrode only.[2] This method of leading is comparable to the method now widely used for recording the so-called chest leads in man, where the exploring electrode is placed at some desired point on the precordium and the indifferent electrode is placed on one of the extremities.

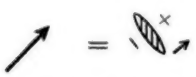
When recording the so-called extremity leads, Lead I is recorded from the upper extremities, Lead II is recorded from the right arm and left leg, and Lead III is recorded from the left arm and left leg. The extremities involved are regarded as mere continuations of the lead wires from the galvanometer. Consequently, the points on the conductor actually under investigation are R at the right shoulder, L at the left shoulder, and F at the symphysis pubis.

With respect to the three points R, L, and F, the electrical forces in the various elements of the accession or the regression wave act as if they were concentrated within a small region at the center of the frontal plane of the body, in the periphery of which the three points lie. Since each force may be represented as a vector,[5] the sum of all forces at an instant must give a vector, the instantaneous cardiac electromotive force of which we may denote by $\hat{E}$. If the instant under consideration is within the auricular or the ventricular accession interval, $\hat{E}$ is known as the instantaneous axis of accession. When the position within the heart (at any instant) of the accession wave is known, it is an easy matter to construct $\hat{E}$ in the proper direction in space with a proportional magnitude. Let us suppose that the accession wave at an instant is in the form of half a tennis ball, expanding outward through cardiac muscle from a point of stimulation. The cut edge of the tennis ball corresponds to the circular boundary of the wave which necessarily resides at the surface of the muscle mass in which the wave is traveling. In effect, the source is distributed over the advancing surface of the wave (outer surface of the hemishell), and the sink is distributed over the trailing surface of the wave (inner surface of the hemishell). We next consider the imaginary plane surface denoted by S, which is circum-

scribed by the wave boundary (cut edge of the hemishell). The imaginary plane, S, is regarded as polarized in a sense similar to that of the wave. $\hat{E}$ always lies perpendicular to S, and is directed away from the negative, toward the positive, side of S. The length or magnitude of $\hat{E}$ is then constructed equal in units of length to the area of S in units of area. By construction, it is clear that the instantaneous cardiac electromotive force $\hat{E}$ is independent of the configuration of the surface of the accession wave, and depends, in a proportional way, only upon the position in space of, and the plane area included by, the boundary of the wave. The foregoing construction is summed up in the simple and important relation[8]

(2-18)*... $$\hat{E} = S\hat{e},$$

or



*It is desired to know the effect upon the extremity leads of an arbitrary open double-layer. For this purpose let us assume that the extent of the conductor (body trunk) is limited to the volume of a large sphere of radius R (Fig. 2, *c*). The effect of the limiting surface of the conductor upon the value of the potential is such that the latter must be distributed everywhere within the interior and yet vanish everywhere outside. The potential of a doublet in an infinite conductor is described by relation (2-6). From this relation an expression may be obtained which satisfies the given boundary conditions. A fundamental equation of theoretical physics states that the electric intensity $\hat{E}$ is equal to the negative gradient of scalar potential; that is,

(2-12) ... $$\hat{E} = -\nabla V$$

where, for our present purpose, the operator del is equivalent to

$$\hat{r}_1 \frac{\delta}{\delta r} + \hat{\theta}_1 \frac{\delta}{r \delta \theta}.$$

Here, $\hat{r}_1$ and $\hat{\theta}_1$ are unit vectors in the directions of r, increasing, and θ, increasing, respectively. Thus the components of the electric intensity are given by the expressions

$$E_r = -\frac{\delta V}{\delta r}, \text{ and } E_\theta = -\frac{\delta V}{r \delta \theta}.$$

Eqn(2-12) shows that, if the electric intensity vanishes, the potential vanishes. For the large spherical conductor of radius R, the component of the gradient in the direction of θ, increasing, is, by symmetry, everywhere tangent to the surface of the conductor. Thus, in order to adapt eqn(2-6) to the given boundary conditions, we have only to consider the component of the gradient in the direction of r increasing. That is,

(2-13) ... $$E_r = -\frac{\delta V}{\delta r} = -\frac{\delta}{\delta r}\left(\phi \frac{\cos\theta}{r^2}\right) = 2\phi \cos\theta \frac{1}{r^3},$$

and, if the right-hand member is to vanish when R = r, we must have for our solution an expression which, when differentiated with respect to r, gives $2\phi \cos\theta/r^3 - 2\phi \cos\theta/r^3$. Moreover, eqn(2-13) shows that our original solution is the first term of the solution sought. For the second term let us try $\phi \cos\theta \frac{2r}{R^3}$. Then

$$-\frac{\delta}{\delta r}\left(\phi \cos\theta \frac{2r}{R^3}\right) = -2\phi \cos\theta \frac{1}{R^3}.$$

Consequently,

(2-14) ... $$V = \phi \cos\theta \frac{1}{r^2} + \phi \cos\theta \frac{2r}{R^3}$$

$$= \phi \cos\theta \left(\frac{1}{r^2} + \frac{2r}{R^3}\right),$$

and is the solution sought. Let us now replace the doublet in the spherical conductor by the arbitrary curved surface of accession double-layer S. For simplicity we may assume that the boundary of the double-layer is circular, and thus circumscribes a plane area S, the center of which coincides with the center of the large conductor. Actually, it is immaterial whether the contour of the double-layer is curved or plane or of some other form, or whether its boundary is circular or of some other form.

(Footnote continued on next page.)

where $\hat{E}$ appears as a vector and S as the magnitude of the unit vector $\hat{e}$, drawn in the direction of the outward normal to the positive surface of S. Having determined $\hat{E}$ in this manner, it is an easy matter to visualize geometrically the effects produced by $\hat{E}$ at the instant under consideration on the potential differences recorded in the three extremity leads.

In any instant at which $\hat{E}$ exists, the effect on the extremity leads is described, in a proportional way, by the projections of $\hat{E}$ upon the lines of the leads. To illustrate, let the so-called lead lines, RL for Lead I, RF for Lead II, and LF for Lead III, form a triaxial reference system (Fig. 2, *d*). The reference axes are seen to divide the frontal plane of the body into sextants. Each reference axis has a positive and a negative half, divided by the origin O. The factor which determines the sense of the half-axes is the arbitrary method adopted for recording the "standard" extremity leads. Thus, the method adopted for recording Lead I is such that, when the potential at L is positive with respect to the potential at R, the potential difference recorded produces an upward (positive) movement on the completed record. Likewise, if the potential at L is negative with respect to that at R, the potential difference recorded produces a downward (negative) movement on the

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The elementary potential dV_a at any field point nearby is, according to eqn(2-9), given by

$$dV_a = (\phi_1 + \phi_2)\,\frac{\cos\theta}{r^2}\,ds$$

Here, the plane area S over which integration is to be performed is equivalent to the open spherical surface of double-layer, inasmuch as their boundaries are coincident and the strength and polarities of each are respectively identical. For the potential at any point in the conductor of radius R we have[3]

(2-15) . . . $$dV_a = \phi\,\cos\theta\,\left(\frac{1}{r^2} + \frac{2r}{R^3}\right)\,ds$$

where ϕ in this relation is taken for $\phi_1 + \phi_2$. Since we are interested only in values of the potential at points upon the surface of the conductor where r = R, eqn(2-15) reduces to[3]

(2-16) . . . $$V_a = \frac{3\phi}{R^2}\iint_S \cos\theta\,ds$$

Let V_1 and V_2 denote the values of the potential at the field points p_1 and p_2, respectively, and let p_1 and p_2 be chosen at the termini of the diameter of the spherical conductor which passes normal to, and through the center of, S. Moreover, let p_1 and p_2 be chosen in such a way that when one is stationed first at the former, and then at the latter, point, upon looking along the diameter, he views first the source and then the sink of the accession double-layer. The electromotive force $\hat{E}$ across p_1 and p_2 may now be determined from eqn(2-16). By definition, the magnitude of $\hat{E}$ is $V_1 - V_2$. Also,

$$V_1 = \frac{3\,\phi}{R^2}\iint_S ds$$

and

$$V_2 = -\frac{3\,\phi}{R^2}\iint_S ds\ .$$

The value of $\cos\theta$ in these expressions is unity and minus unity, respectively. Thus, the relation which describes the electromotive force of the accession double-layer is

(2-17) . . . $$\hat{E} = \frac{6\,\phi\,S}{R^3}\,\hat{e}\ .$$

where S is the plane area or analytic surface circumscribed by the boundary of the accession double-layer, and $\hat{e}$ is a unit vector in the direction of the outward drawn normal to the positive surface of S. In eqn(2-17) $\hat{E}$ has the direction of $\hat{e}$ and the magnitude $6\phi S/R^3$. If we neglect the constant $6\phi/R^3$, we obtain the simple relation

(2-18) . . . $$E = S\hat{e}$$

which is useful in defining (in a proportional way) the electromotive force of accession. Here, E is equal in units of length to the area of S in units of area.

completed record. If the potential at F is positive with respect to that at R or at L, the potential differences recorded in Leads II and III produce upward (positive) movements on the completed record.

Let us suppose that $\hat{E}$ in Fig. 2, *d* is proportional to the accession electromotive force at a given instant. The projections of $\hat{E}$ upon the three reference axes describe the potential differences V_1, V_2, and V_3. The movement in all three leads is upward (positive) and is greatest in Lead II and smallest in Lead III. In order that $\hat{E}$ in the reference plane may describe the full value, proportionally, of the effects of the accession wave, the boundary of the wave must lie in some plane perpendicular to the plane of the reference system. Inasmuch as the boundary of the wave is not restricted in this manner, the vector $\hat{E}$ is not restricted to the plane of the reference system. In order to indicate the electromotive force which is not restricted to the plane of the reference system, we may prefix the letter s before the vector, indicating a spatial axis (free to move in three-dimensional space). Accordingly, the vector $\hat{E}$ is always taken as the projection of $s\hat{E}$ upon the plane of the triaxial reference system. Obviously, if $s\hat{E}$ is normal to the frontal plane, $\hat{E}$ is zero. Consequently, electromotive forces directed normal to the frontal plane of the body do not affect the extremity leads. In the particular case in which $s\hat{E}$ lies in the frontal plane, $\hat{E} = s\hat{E}$.

We are now in position to ascertain the effects on the extremity leads which occur during cardiac accession. Let us simplify the problem by substituting for the heart a spherical mass of cardiac muscle (Fig. 2, *e*). Let us suppose that stimulation occurs at A. Successive positions of the wave boundary appear in the order numbered as the wave approaches B. Here, the points A and B are regarded as lying in the triaxial reference plane, so that $s\hat{E} = \hat{E}$. Moreover, the magnitude of $\hat{E}$ increases progressively, reaching a maximum at the time at which the boundary of the wave forms a great circle. Thereafter, the magnitude of $\hat{E}$ decreases progressively to become zero as the wave reaches B. The direction of $\hat{E}$ is constant during the accession interval, and is such that $\hat{E}$ occupies the sixth sextant. During the accession interval, the terminus of $\hat{E}$ may be regarded as tracing out a segment of the line AB twice, commencing and ending at the origin O of the triaxial reference system.

Keeping the foregoing factors in mind, the potential differences produced on the extremity leads throughout the accession interval may be visualized by inspection of Fig. 2, *d*. The form of the deflections is shown in Fig. 2, *f*. Each group of three potential differences determined on the triaxial reference system by a given magnitude of, and direction of, $\hat{E}$ defines a group of three simultaneous ordinates under the curves of Leads I, II, and III. As the actual accession wave progresses in the heart, $s\hat{E}$ varies continuously in magnitude and direction throughout three-dimensional space.

SECTION III

FURTHER CONSIDERATIONS OF CARDIAC ACCESSION

The present state of our knowledge of the path by which the accession wave spreads over the heart permits only an approximation of the manner in which the P and QRS deflections are formed. There appear to be at least three distinct advantages, however, in attempting an approximation or synthesis of the kind herein undertaken. It will serve, first of all, as the introduction of a method by which a more detailed synthesis can be made when more data are known; it will serve, secondly, as a means of pointing out the more important factors upon which the form of the accession deflections depends; and, thirdly, it will offer a reference scaffold with respect to which certain valuable inferences may be drawn regarding the abnormal electrocardiogram.

Let us assume that the position of the heart within the chest is normal, and halfway between the vertical and horizontal; that the specific conductivity of the body is normal; that the normal order of accession occurs; and that the order is known. It then becomes possible to estimate the proportional magnitude and direction in space of the instantaneous axis $s\hat{E}$ of cardiac accession at various critical moments during the accession (P and QRS) intervals. These data will, in turn, give the imaginary path described in space by the terminus of $s\hat{E}$. The path thus described during the auricular accession interval is called the P $s\hat{E}$-loop, whereas the path described during the ventricular accession interval is called the QRS $s\hat{E}$-loop. These loops, including the T $s\hat{E}$-loop, are referred to collectively as the vectorcardiogram. When their form has been determined analytically it is an easy matter to visualize geometrically the form of the extremity leads.

QRS

The accession wave invades the junctional tissues (A-V node, His bundle and branches, and the Purkinje network) during the downstroke of the P deflection. This fact is obvious, for the A-V node must be reached at the time when auricular accession is approximately half complete. The velocity of the accession process through the Purkinje network has been estimated at ten times that at which it spreads through the auricular muscle.

Let us consider further the relation,

$$(2\text{-}18)\ldots \qquad s\hat{E} = S\hat{e},$$

where $s\hat{E}$ is the spatial cardiac electromotive force; S is the imaginary plane circumscribed by the boundary of the ventricular accession wave, and is considered polarized in the same sense as the wave; and $\hat{e}$ is a unit vector in the direction of the outward drawn normal to the positive surface of S. When two or more vectors are added to give a resultant vector, the members of the sum are referred to as the components of

the resultant vector. A vector is, therefore, equal to the sum of all its components. Thus if

$$(3\text{-}1)\ldots \qquad s\hat{E} = S_1\hat{e}_1 + S_2\hat{e}_2 + S_3\hat{e}_3 \ \ldots \text{etc.}$$

each member on the right-hand side is a vector quantity representing a component of the resultant electromotive force $s\hat{E}$. Each of the analytical areas S_1, S_2, S_3 ... etc., is circumscribed by a separate boundary of the accession wave. The number of these boundaries existing simultaneously determines numerically the number of such areas. On the other hand, $\hat{e}_1$, $\hat{e}_2$, $\hat{e}_3$, ... etc., are unit vectors drawn in the direction of the outward normals to the respective positive surfaces of the analytical areas.

During the brief period in which the accession wave is passing through the junctional tissues, there is an analytical area S in the cross section of each Purkinje fiber, and the cardiac electromotive force $s\hat{E}$ is given according to eqn (3-1); that is, by the sum or resultant of all such component forces existing at the instant considered. There appears to be no related displacement of the galvanometer fiber during the conduction interval. Presumably, the magnitude of $s\hat{E}$ is insufficient to affect the completed record. It follows directly that the onset of QRS occurs shortly after the instant at which the accession wave begins to invade the ventricular muscle.

Let us assume that ventricular stimulation takes place at many points simultaneously upon the endocardial surface of the ventricular muscle. An accession wave of hemispherical form must then develop about each point of stimulation. The boundaries of the many waves thus formed define as many analytical areas which may be looked upon as so many subendocardial islets.

If some of the Purkinje fibers have pierced the ventricular muscle, they lead to deep points of stimulation. Each of the accession waves which form about the deep points of stimulation must have the form of a spherical, closed surface. Each such surface must remain closed until it reaches, by expansion, the limiting surface of the resting muscle mass in which it is traveling. As long as the many spherical surfaces of accession remain closed, they can make no contribution to the heart's electrical field. In this respect the closed accession surfaces under consideration act in a way altogether similar to the single resting or excited cell. Consequently, the total effect will be the same, or nearly the same, as it would if stimulation took place at subendocardial points only.

A short interval later, the subendocardial islets become confluent, at which time two large shells, S_R and S_L (for the right and the left ventricle, respectively), are formed by the now continuous contour of the accession wave. The contour of either shell must be very nearly that of the homolateral endocardium, and have boundaries approximately coincident with those of the four valve openings. The four boundaries

thus indicated may be looked upon as forming a single analytical surface, S_1, circumscribed by the inner edge of the auriculoventricular junction. Clearly, the positive surface of the analytical area S_1 is directed toward the ventricular apex.

If the distribution of the points of ventricular stimulation is not uniform, there must be a greater density of islets in the regions to which the distribution of Purkinje fibers is most dense. No such subendocardial regions have been demonstrated as yet, and we shall, therefore, omit a consideration of them. On the other hand, if some region of subendocardial muscle is stimulated relatively early, this region must have islets of relatively greater circumference.

For the moment, let us assume that there are no such regions of early stimulation. Consequently, all of the islets must have the same dimensions simultaneously. This is equivalent to regarding the area S_1 as made up of uniformly scattered particles, or of a uniform density. Before the subendocardial islets appear, the density of S_1 is zero. When the subendocardial islets expand and become confluent, the density of S_1 is unity. Consequently, the density, D, of S_1 may be regarded as increasing from zero to unity throughout the initial phase of ventricular accession. The electrical effect of the initial phase is defined by the relation

$$s\hat{E} = D(S_1\hat{e}_1) \qquad (3\text{-}2)\ldots$$

where $\hat{e}_1$ is a unit vector drawn in the direction of the outward normal to the positive surface of S_1. During the initial phase of ventricular accession it appears that the magnitude of $s\hat{E}$ increases from zero to S_1, at the end of which time the shells S_R and S_L are intact. Consequently, the terminus of $s\hat{E}$ traces out a path which is collinear with a line drawn from the center of the ventricular base toward the apex; that is, from the origin O of the triaxial reference system into the sixth sextant.

Anatomic studies have shown[9] that the left main branch of the His bundle gives off "early" branches which supply the anterior basal region of the interventricular septum. There are no "early" branches of the right main branch of the His bundle. The right main branch travels for a considerable distance toward the apex of the right ventricle before giving off branches to the septum. From this it may be concluded that the specified subendocardial region of the left septal surface is a region of relatively early stimulation. The islets of this region are, therefore, of relatively large circumference during the initial phase of ventricular accession. The component electromotive forces generated by the region of early stimulation are directed, in the sthenic adult, upward and forward, toward the sternum. Because of the preponderance of the early septal forces, the initial segment of the QRS $s\hat{E}$-loop bends in a nearly similar direction, after which the loop courses downward and to the left in its previously described direction toward the ventricular apex.[10]

During the subsequent, brief period of ventricular accession, the shells S_R and S_L expand in the direction of the ventricular epicardium and toward each other within the septum. The expansion is attended by a relatively small increase in the area S_1, with a further motion of the terminus of $s\hat{E}$ toward the ventricular apex. Expansion of the shells continues until one of the shells makes contact with the epicardial surface at a point where the subjacent ventricular wall is thinnest. Let us assume that this point is on the anterior aspect of the right ventricle, about halfway from base to apex. At the epicardial point specified, the shell S_R necessarily develops a new boundary which, on further expansion of the shells, must itself expand rapidly in all directions over the anterior aspect of the ventricular chambers, only to converge promptly over the posterior aspect of these chambers toward a second, posterior, epicardial point, located where the subjacent ventricular wall is thickest.

We may denote by S_2 (Fig. 3, *b*) the plane analytical area circumscribed by the new boundary. Obviously, the positive surface of S_2 is directed toward the spine. Whenever the first and second analytical areas exist, $s\hat{E}$ is defined by the relation

$$s\hat{E} = S_1\hat{e}_1 + S_2\hat{e}_2. \qquad (3\text{-}3)\ldots$$

On first thought, the boundary of the second analytical area may appear to become confused with that of the first as the former sweeps over the epicardial surface of the ventricles. Let us consider the points of contact of the two closed curves. At first contact, there is only one such point, then two, and finally one again. At any instant when two points exist (see Fig. 3, *b*), we may connect them with the line AB and note that AB forms a common boundary segment closing both of the boundaries of S_1 and S_2. In this way it may be observed that the dorsal motion of the second analytical area S_2 results in decay of the first analytical area S_1.

Clearly, the circumferential variations of the areas S_1 and S_2 must, according to eqn(3-3), cause the terminus of $s\hat{E}$ to part from its course in the direction of the ventricular apex and sweep in a dorsal direction, at first increasing its distance from the origin, and then decreasing this distance to zero as the final direction of $s\hat{E}$ becomes that of a line drawn from the center of the heart toward a point on the posterior epicardial surface where the area S_2 vanishes.

It is possible in this manner to construct synthetically the path described in space by the terminus of $s\hat{E}$ during the QRS or ventricular accession interval. The path is the QRS $s\hat{E}$-loop of the vectorcardiogram. The projection of the loop upon the triaxial reference plane (Fig. 3, *c*) is the QRS $\hat{E}$-loop of the vectorcardiogram. The figure also illustrates the relationship of the QRS $\hat{E}$-loop to the form of the QRS complex of the extremity leads.

An excellent idea of the position in space of the QRS sÊ-loop may be gained by bending a pipe cleaner into the form of the loop and casting a distant light upon it, so that its shadow is thrown upon a card upon which a triaxial reference system has been described.

Let us define the anatomic axis of the heart as a vector, ĥ, drawn from the center of the ventricular base toward the ventricular apex.

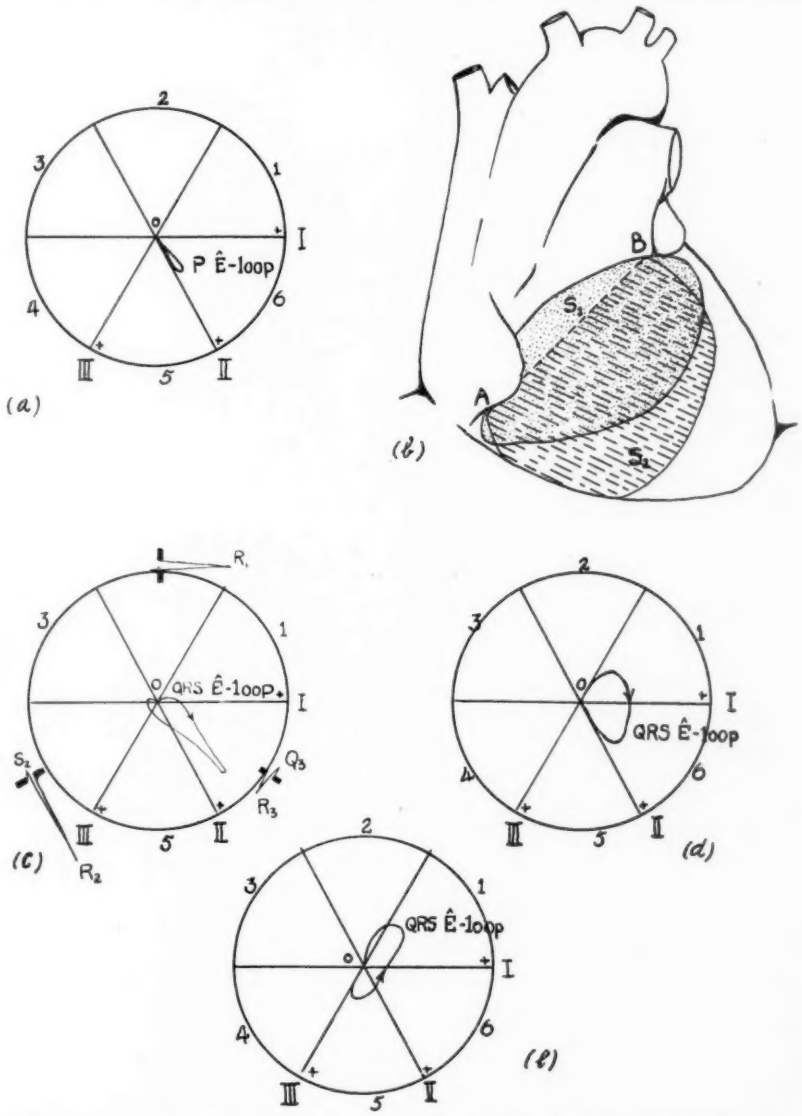


Fig. 3.—(*a*) Projection of the auricular accession effects upon the triaxial reference plane. They constitute the P ê-loop of the vectorcardiogram. (*b*) The analytical surfaces, or areas S_1 and S_2 of normal ventricular accession. (*c*) Showing the relationships between the QRS ê-loop of the vectorcardiogram, the triaxial reference system, and the associated deflections of the extremity leads. (*d*) and (*e*) Depicting the form of the QRS ê-loop as altered, respectively, by posterior and anterolateral infarcts. See text.

Positive rotation of the ventricles about ñ is regarded as that motion which appears counterclockwise to an observer stationed at the terminus of ñ, whereas negative rotation of the ventricles appears clockwise. It is highly advisable to study, in the manner suggested, the effects upon QRS of the extremity leads produced by elevation and fall of the free extremity of the loop. These motions will serve to explain clearly the highly complex variations of QRS of the extremity leads caused by motion of the heart as the result of breathing.

VENTRICULAR HYPERTROPHY AND BLOCK

An increase in the thickness of the ventricular walls affects the order of ventricular accession, or the form of QRS. The part played by this factor may be easily reasoned from a consideration of the part played by the normal thickness of the ventricular walls. It should be pointed out, however, that hypertrophy of one or both ventricles may produce a significant change of position of the ventricular mass, and thereby alter the form of QRS in this manner also.

Variations, whether normal or abnormal, in the architecture of the Purkinje network alter the manner of ventricular stimulation, the order of ventricular accession, and the form of QRS. The abnormal variations in the network are responsible for QRS changes ascribed to intraventricular block.

At times it is difficult, if not impossible, to ascertain whether one or a combination of factors, hypertrophy and block, is responsible for the QRS changes encountered. In any event, the ventricular accession interval is prolonged. Data on the velocity of the ventricular accession wave suggest that hypertrophy of the ventricles rarely prolongs the QRS interval beyond 0.10 second. Apparently, hypertrophy of the normally thin right ventricle rarely prolongs the QRS interval beyond 0.09 second.

In general, hypertrophy tends to produce an increase in the amplitude of certain of the QRS deflections, whereas intraventricular block tends to produce marked slurring and notching of these deflections.

During the analysis of bundle branch block curves, it is all-important to remember that, in the initial stages of ventricular accession, only the contralateral shell develops and is responsible for the initial QRS deflections. During the final stages, no homolateral shell develops because of the abnormal manner of (retrograde) stimulation. Thus, the broad, final QRS deflections are written by the abnormal accession of the homolateral ventricle.

ON LOCAL MUSCLE DESTRUCTION (INFARCTION)

Destruction of ventricular muscle, recent or old, local or diffuse, complete or incomplete, results in an absence, during accession, of electrical forces which were previously present within the dead region. The

character of the associated QRS changes depends, quite generally, upon the location and degree of the damage. For example, diffuse damage or fibrosis of uniform degree may be regarded as diminishing proportionally the numerical values of the analytical areas of ventricular accession, thus diminishing, in turn, the amplitude of the associated accession deflections without extensively changing their form.

On the other hand, the limits of a localized, severely damaged region define, at some time during accession, a new and abnormal boundary for one or both of the shells S_R and S_L, according to the points of contact of the shell or shells with the limits of the damaged region. Each new and abnormal boundary circumscribes a new and abnormal analytical area which, in turn, accounts for a new and abnormal component of the electromotive force $s\hat{E}$. Each component thus created supplies an additional term to the right-hand member of relations (3-2) and (3-3), according to when the new force exists.

It may appear paradoxical that the presence of a dead region, which is electrically inert, is accounted for by the addition in this manner of a new component electromotive force. The force arises, however, in consequence of the now unopposed forces in the diametrically opposite region of the involved shell. As a matter of fact, the new and abnormal force is itself the resultant of the newly unopposed forces of the involved shell.

Let us use the expression $S_3\hat{e}_3$ to describe an abnormal electromotive force of the kind under consideration. The analytical area S_3 is circumscribed by the boundary of the accession wave at the points of contact of the wave with the limits of the dead region. The positive surface of S_3 is directed toward the center of the involved ventricle, and $\hat{e}_3$ is a unit vector in the direction of the outward drawn normal to the positive surface of S_3. Thus the direction of the new and abnormal electromotive force $S_3\hat{e}_3$ is along a line drawn from the center of the dead region toward the center of the involved ventricle. For example, if it is now assumed that the dead region is essentially subendocardial, the ventricular accession axis $s\hat{E}$ is defined, throughout the initial phase of accession, by the relation

$$(3\text{-}4)\ldots \qquad s\hat{E} = D(S_1\hat{e}_1 + S_3\hat{e}_3).$$

The frequent occurrence of local death in certain regions of the ventricular muscle makes them of particular importance, and they are considered separately in the discussion which follows.

The first region considered is ordinarily irrigated by subdivisions of the right coronary artery, and includes that part of the left ventricular wall which is adjacent to the diaphragm and the neighboring portion of the basal region of the interventricular septum. Infarction of this region is herein referred to as posterior infarction. As a general rule, infarction of the ventricular muscle involves at least the subendocardial half of the wall of the left ventricle, and, when the in-

volvement is transmural, the extent as observed from the epicardial surface is considerably less than when observed from the endocardial surface. The limits of a posterior infarct are ordinarily such that the hole cut out of S_L defines an area S_3, with its positive surface directed upward, forward, and somewhat to the left, toward the center of the left ventricle. The projection of the new and abnormal force $S_3\hat{e}_3$ upon the plane of the triaxial reference system gives a vector which is directed into the first or second sextant. The preponderance of force in this direction distorts the initial stroke of the QRS $\hat{E}$-loop into the first sextant (see Fig. 3, *d*). The initial stroke of the QRS $\hat{E}$-loop, as it sweeps into that part of the first sextant which is adjacent to the second, writes the upstroke of R_1 and the downstroke of Q_2 and Q_3. If the initial segment of the loop had swept into that half of the first sextant which is adjacent to the sixth, because of more septal and less diaphragmatic wall involvement, the initial phase of the QRS complex would have been characterized by $R_1R_2Q_3$ deflections. The magnitude of the abnormal force $S_3\hat{e}_3$ depends chiefly on the circumferential limits of the dead region, and, therefore, these limits are related proportionally to the amplitude of the abnormal Q_2Q_3 deflections. The duration of the force $S_3\hat{e}_3$ is primarily proportional to the extent of the infarct in the direction of the epicardial surface of the diaphragmatic wall and the right ventricular endocardial surface of the septum. Because a majority of posterior infarcts extend halfway or more through the wall, a significant Q_3 is taken as 0.04 second or more in duration.[11] Transmural infarcts of the posterior type may produce a single downward movement for QRS_3, a so-called QS_3 deflection. R_1 and Q_2 deflections are likewise present. It may safely be stated that many small posterior infarcts are not accompanied by characteristic $R_1Q_2Q_3$ deflections because of the small magnitude of the component force $S_3\hat{e}_3$. For an example of these QRS changes, see Fig. 4, *a*.

The second region considered is ordinarily irrigated by the anterior descending branch of the left coronary artery and is located in the anterolateral wall of the left ventricle. Infarction of this region is herein referred to as anterolateral infarction. The hole cut out of the shell S_L by the dead region defines a new and abnormal analytical area, S_4, with its positive surface directed downward, backward, and somewhat to the right, toward the center of the left ventricle in such a way that the associated, abnormal component $S_4\hat{e}_4$ (as projected upon the triaxial reference plane) distorts the initial segment of the QRS $\hat{R}$-loop into the fourth or into the adjacent half of the fifth sextant (Fig. 3, *e*). The associated QRS complexes are characterized by initial $Q_1R_2R_3$ deflections. As shown in Fig. 3, *e*, R_1 is usually of small, whereas S_2 and S_3 are usually of large, amplitude. An essentially apical infarction of the region specified may cause the initial segment of the loop to sweep into that part of the fourth sextant which is adjacent to the third, thus producing a $Q_1Q_2R_3$ variety of initial QRS deflections.

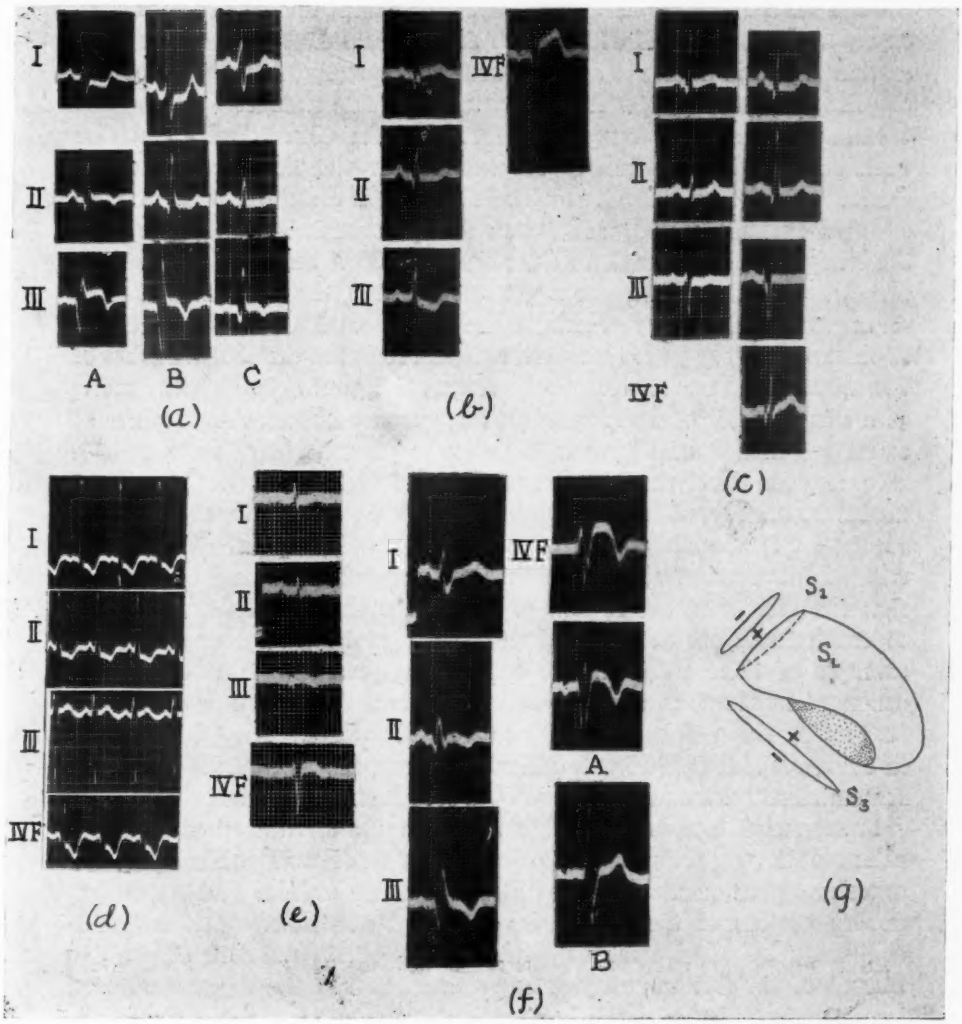


Fig. 4.—(*a*) Curves A and B were recorded nine months apart from a subject who had had a relatively recent posterior infarct. QRS is of the $R_1Q_2Q_3$ variety. Curve C was recorded from the same subject shortly after anterolateral infarction had developed. Note the reduction in amplitude and the slurring of R_1, and the greatly reduced amplitude of Q_2 and Q_3. At autopsy, both infarcts were seen to involve only the endocardial half of the ventricular wall. (*b*) A curve recorded on the day of death from a subject with hypertensive heart disease. The form of the curve illustrates changes caused by recent anterolateral infarction. At autopsy, the diameters of the infarct measured 7 cm. and 4 cm., respectively, on the endocardial and epicardial surfaces. (*c*) Curves recorded before and after the occurrence of strictly anterior infarction. The last attack of coronary pain had occurred one week before the right-handed recording. The Q_4 and the subsequent notch indicate that the precordial position 4 is superjacent to the margin of the infarct. Autopsy revealed that death had resulted from carcinomatosis of the liver. The healed, strictly anterior infarct measured 2.5 cm. in diameter and was confined to the endocardial half of the wall. (*d*) The clinical picture was characteristic of acute myocardial infarction. The changes are not considered diagnostic. However, the absence of QRS changes, together with the clinical picture, suggests that the infarct may be strictly anterior or posterior. The nature of the RS-T junction displacements (if due to injury) suggests involvement of the posterior wall. Preponderant hypertrophy of the left ventricle is probably responsible for all the changes shown. (*e*) Illustrating the changes associated with massive apical infarction. The minute R_4 may be ascribed to activation of the living subendocardial layer. At autopsy a few weeks after the recording, the large apical infarct was found to be of the transmural variety. (*f*) The changes are considered diagnostic of recent large posterior infarct and complete right bundle branch block. (*g*) Illustrating the manner of production of the QRS changes shown in (*f*). See text.

On the other hand, if an infarct of anterolateral location is somewhat basal, the first segment of the loop sweeps into that part of the fifth sextant which is adjacent to the fourth, and, consequently, Q_1 is of low amplitude. See Fig. 4, *b* for an example of these changes.

Inasmuch as newly unopposed forces in the diametrically opposite ventricular wall are directly responsible for the new and abnormal electromotive force associated with infarct, it is clear that the presence of the abnormal force depends, not only upon the infarct, but also upon the integrity of that region of the wall in which the newly unopposed forces lie. If, in addition to a posterior infarct, there is assumed to be an anterolateral infarct of similar dimensions, and the two infarcts are of diametrically opposite location, analysis requires the consideration of two new and abnormal component forces, $S_3\hat{e}_3$ and $S_4\hat{e}_4$. Furthermore, as a direct result of these assumptions, the two abnormal forces are of equal magnitude and inverse direction. Consequently, their sum is zero, and the effect produced on the form of QRS by the former, is annulled by that produced by the latter, infarct. Likewise, the effect of the latter, is annulled by the effect of the former, infarct. To be more exact, however, a result of this kind requires the additional assumption that the corresponding regions of the myocardium which are adjacent to the infarcts are activated simultaneously. Clinically, of course, an example of this sort is almost out of the question. It is reasonably common, however, to see typical QRS effects of one infarct annulled in part by the occurrence later of a second infarct. The QRS changes in curves B and C of Fig. 4, *a* illustrate just such a sequence of events. A "staircase" descending limb of Q_3 is occasionally produced.

A somewhat less common region for the site of infarction is the so-called strictly anterior region of the ventricular wall, made up of the anterior apical portion of the interventricular septum and the neighboring portion of the free wall of the left ventricle. This region is ordinarily irrigated chiefly by subdivisions of the anterior descending branch of the left coronary artery. Infarction of the region indicated is conveniently called strictly anterior. The hole cut out of S_L by the dead region defines an abnormal analytical area S_5, with its positive surface directed posteriorly toward the center of the left ventricle. The new and abnormal component $S_5\hat{e}_5$ is perpendicular to the plane of the triaxial reference system. Consequently, its projection upon the frontal plane is zero, and there are no associated changes in the form of QRS of the extremity leads. The reader is referred to Fig. 4, *c* for an example of a curve of a strictly anterior infarct.

Of relatively rare occurrence is infarction of the strictly posterior wall of the left ventricle. The region involved is near the ventricular base. Its diametrically opposite position with respect to the apical portion of the septum has led some observers to refer to its infarction as "posterolateral" or "lateral." Infarcts in this region are more properly called strictly posterior infarcts. The muscle involved is ordinarily irrigated chiefly by subdivisions of the circumflex branch

of the left coronary artery. Like the case of strictly anterior infarct, the hole cut out of S_L by the strictly posterior infarct defines a new and abnormal area S_6, coplanar to the plane of the triaxial reference system. The associated abnormal component $S_6\hat{e}_6$ is directed anteriorly toward the center of the left ventricle, perpendicular to the plane of the reference system. Its projection upon the plane is consequently zero, and no associated changes appear in QRS of the extremity leads. See Fig. 4, *d* for an example.

Occasionally, infarction may involve the entire apex of the left ventricle. The new and abnormal component $S_7\hat{e}_7$ has the inverse direction of $S_1\hat{e}_1$, and the former, therefore, tends to nullify the effects of the latter. When, in addition, it is recalled that the other component $S_2\hat{e}_2$ of normal accession acts chiefly in a direction perpendicular to the frontal plane of the body, it becomes obvious that apical infarction tends to establish an equilibrium of effective forces of ventricular accession. Consequently, the QRS $\hat{E}$-loop and its associated QRS deflections are characteristically of small dimensions (see Fig. 4, *e*).

In all of the above-mentioned varieties of infarction the shell S_L is involved. The failure of infarction to effectively involve the shell S_R is due presumably to the thinness of the wall of the right ventricle. Various studies on the coronary circulation indicate that a considerable volume of return coronary flow reaches the cavity of the right ventricle through numerous thebesian veins. It is held that, when the intra-arterial pressure falls as a result of diminished coronary flow, a reverse irrigation of the free wall of the right ventricle through the thebesian veins markedly diminishes the incidence of infarction of the free wall of the right ventricle. The interventricular septum, however, enjoys no such freedom from infarction, and is, therefore, best regarded as a complement of the free wall of the left ventricle.

The foregoing discussion places great importance on the initial QRS deflections in the diagnosis and location of infarction. The justification is primarily due to the consistent manner in which the electromotive force $S_1\hat{e}_1$ develops during the early stages of ventricular accession. The very nature of the development of the second component $S_2\hat{e}_2$ of normal ventricular accession makes for rather wide variability of the final QRS deflections of the extremity leads under normal as well as abnormal circumstances. Consequently, changes in the form of the final QRS deflections are of relatively little value in the diagnosis or location of infarction.

For a detailed example of the application of the analytical principles herein introduced, let us consider Fig. 4, *f*. The patient from whom the electrocardiogram was recorded was a white man, aged 52 years, who had been asymptomatic until he suddenly developed the clinical picture of acute cardiac infarction twenty-four hours before, and died five days after, the recording.

The duration of QRS is 0.12 second and S_1 is prominent and broad.

These changes are sufficient to justify the diagnosis of complete block of the right main branch of the His bundle.[12] When the right main bundle branch is blocked, the left ventricle undergoes accession first, and the order of accession is locally normal. Under these circumstances, the left ventricle may be regarded as writing the initial QRS deflections. Moreover, infarction must have the same, or nearly the same, effect upon the initial QRS deflections as it would have if right bundle branch block were not present. Inspection of Leads II and III shows conspicuous Q_2 and Q_3 deflections of the kind described as characteristic of posterior infarction. The fact that the duration of Q_3 is one-half as long as the duration of QRS suggests that the subendocardial infarct extends about halfway through the ventricular wall. The smooth, prominent downstroke of Q_3 suggests that the anterolateral wall of the left ventricle is intact. The electrical situation which underlies these changes is depicted in Fig. 4, *g*. The area S_1 is reduced to about half of its normal magnitude because of the absence of the shell S_R. The new and abnormal area S_3 is defined by the circumferential limits of a large infarct in the septum. Throughout the initial stages of ventricular accession, the cardiac electromotive force is defined by the relation

$$s\hat{E} = D(S_1\hat{e}_1 + S_3\hat{e}_3).$$

The initial segment of the QRS $\hat{E}$-loop sweeps into the adjacent halves of the first and second sextants and is approximately collinear with the negative Lead III reference axis. Analysis of the precordial leads and of the final ventricular deflections shown in Fig. 4, *f* is presented elsewhere. The autopsy observations are described in the legend.

A situation which is decidedly different from the one cited above exists for the analysis of left bundle branch block, in which the initial QRS deflections are of little or no help in the diagnosis of infarction. Here, the onset of QRS is of the $R_1R_2R_3$ variety, primarily because of the development of the shell S_R. If a small Q_1 is present, the block of the left side may be incomplete. It is conceivable that a $Q_1R_2R_3$ variety might be produced by the combination of left bundle branch block and a transmural infarct of the interventricular septum.

ON SEMIUNIPOLAR AND UNIPOLAR LEADS

When the two terminals of the galvanometer are connected with the body in such a way that one electrode is near the heart (upon the precordium) and the other is at a distant point (upon an extremity), the completed curve represents chiefly the fluctuations of the potential at the field point near the heart. The near contact is called the exploring electrode and the distant contact is called the indifferent electrode.

There are a considerable number of accepted methods of contacting the body with the galvanometer when recording semiunipolar and unipolar leads. The methods differ according to the position of the near contact and the position of the distant contact. When one of the ex-

tremities is used for the distant contact, the lead is said to be a semiunipolar lead. When the distant contact is made with a central terminal which is connected in turn to each of the extremities R, L, and F, the lead is said to be a unipolar lead. The notation adopted for the semiunipolar leads is CR, CL, and CF; C indicates that the exploring electrode (placed on the chest) is being paired with an indifferent electrode placed on one of the extremities R, L, or F. When the chest electrode is paired with the central terminal, the letter V designates the method. The precise position of the exploring electrode is designated by numerical subscript inserted after the capital letters or letter, as the case may be. Thus, CF_2 indicates a semiunipolar lead recorded by pairing the chest electrode, placed at the precordial position 2, with an extremity electrode placed on the left leg. In a like manner, V_2 indicates a lead recorded by pairing the chest electrode at position 2 with the central terminal. The accepted precordial positions are as follows. Position 1 is in the fourth intercostal space at the right margin of the sternum. Position 2 is in the fourth intercostal space at the left margin of the sternum. The other positions lie upon a line drawn from position 2 to the lateral margin of the apex beat, or to the junction of the left midclavicular line and the fifth intercostal space when the location of the apex beat cannot be ascertained. The line continues into the axillary region at the level of the junction specified. Position 3 is at the left parasternal line, position 4 is at the midclavicular line, position 5 is at the anterior axillary line, and position 6 is at the midaxillary line. Still another, and perhaps the most popular of the precordial leads, is denoted Lead IVF. Here, the precordial contact is placed just lateral to the apex beat (wherever it is found) and the extremity electrode is placed on the left leg. In all of the foregoing leads it is customary to arrange the galvanometer-body contacts in such a way that a positive potential at the precordial electrode produces an upward movement on the completed record.

The semiunipolar leads are continuously influenced to a variable degree by the fluctuations of the potential at the extremity to which the distant electrode is connected. At times, during interpretation of the semiunipolar leads, it is highly desirable to know the instantaneous potential at the extremity used in the recording. Let us denote by V_R, V_L, and V_F the instantaneous potential at R, L and F, respectively. Then, if

$$\text{LI} = V_L - V_R, \tag{3-5}$$

by the adopted method of leading, we have

$$\text{LII} = V_F - V_R \tag{3-6}$$

and

$$\text{LIII} = V_F - V_L. \tag{3-7}$$

On the assumption that the electrical effects of the heartbeat act as if generated in a small region within the plane of the triaxial reference system, we have (by Kirchhoff's first law)

(3-8) ... $$V_R + V_L + V_F = 0.$$

By adding equalities in eqns(3-5) and (3-6), we get

$$LI + LII = V_F + V_L - 2V_R.$$

But from eqn(3-8) we have $V_F + V_L = - V_R$. Hence, by substitution we get[13]

$$LI + LII = - 3V_R$$

or

(3-9) ... $$V_R = - \frac{LI + LII}{3}$$

for the potential at the right shoulder at an instant in terms of the potential differences in Leads I and II at a simultaneous instant.

In a like manner, we get

(3-10) ... $$V_L = \frac{LI - LIII}{3}$$

and

(3-11) ... $$V_F = \frac{LII + LIII}{3}$$

for the potentials at the left shoulder and at the symphysis pubis, respectively, in terms of simultaneous potential differences in the extremity leads. Obviously, in normal persons, when the heart is vertical and the potential differences are large in Leads II and III, the influence of the extremity potential V_F upon the CF leads may be considerable. In normal persons whose hearts are horizontal and the potential differences are large in Leads I and III, the influence of the extremity potential V_L upon the CL leads may be considerable.[14]

The accession potential at the precordial position is most conveniently defined by the relation (2-9); that is,

$$Va = (\phi_1 + \phi_2)\Omega,$$

where Va is the potential at the precordial electrode, ϕ_1 and ϕ_2 are constants denoting the electrical moments (intensity of polarization per unit of area of wave front) of the accession wave, and Ω is the solid angle defined and measured by the area of spherical surface cut off the unit sphere inscribed about the precordial point by the cone formed by drawing lines from the precordial point to every point upon the boundary of the accession wave. When the accession wave has more than one boundary at the instant considered, a corresponding number of

cones is formed, and the potential is regarded as proportional to the sum of the areas cut off the unit sphere by all the cones. The sense of the potential may be determined in the following way. Let us imagine that the accession wave is opaque, and that it carries a positive charge upon its advancing surface and a negative charge upon its trailing surface. An observer stationed at the center of the unit sphere (or at the tip of the precordial electrode), on looking through the base of the cone, must view the positive or the negative charge on the wave. The sense of the charge observed is the same as the sense of the potential. If multiple cones have been formed because the wave has more than one closed boundary, the observer at the center of the unit sphere looks through the base of one cone at a time, treating the wave as if all of the other cones and related boundaries were absent. The resulting sense of the potential will depend quite naturally upon the relative magnitude of the positive as compared with the negative solid angles. When the former magnitude is larger the sense of the potential is positive.

For example, let us consider the accession shell S_L (Fig. 5, *a*). P denotes the field point at which the precordial potential is measured. Clearly, the sense of the solid angle subtended at P by the boundary of the shell S_L is positive. Moreover, the potential at P would have the same value if all portions of the wave not included by the cone were removed. Consequently, that portion of the wave subjacent to P has a preponderant effect upon the potential at P. The value of the potential at the precordial electrode is determined chiefly by that arbitrary portion of the accession wave (or regression wave) which lies nearest the precordial electrode.[15] This fact renders the interpretation of the unipolar (and semiunipolar) lead relatively simple.

Let us consider first the analysis of a normal curve recorded by Lead IVF. Under the circumstances, the electrical events in the apical regions of the ventricular walls dominate the form of the curve. When there are no electrical events in the subjacent ventricular wall, the form of the curve depends, for the most part, upon events occurring elsewhere. If these are scattered, but equidistant, or nearly equidistant, from the exploring electrode, the potential depends more or less equally upon all such events.

During the early stages of ventricular accession, the solid angle subtended at the tip of the precordial electrode by the boundary of the wave is often small and negative for a brief interval. Thus, a normal Q_4 results (amplitude = 0.2 millivolt or less, duration = 0.01 to 0.02 second). It appears highly probable that this deflection is caused by the relatively early invasion of the anterior basal region of the interventricular septum subjacent to the left ventricular endocardium. A similar Q_4 deflection is often seen normally in the fifth and sixth precordial positions, but not in positions 1, 2, and 3. The validity of the explanation is further supported by the fact that Q_4 occurs regularly in hearts which are the seat of hypertrophy of the left ventricle. The hypertrophy

produces a positive (counterclockwise) rotation of the ventricles about ñ, and brings the endocardial aspect of the septal region specified into better view from the exploring electrode tip, which thus determines a more significant magnitude for the negative solid angle subtended. A Q_4 of this kind should be rare in children and in preponderant hypertrophy of the right ventricle because in these instances the positions of the ventricles are ones of relative negative rotation about ñ.

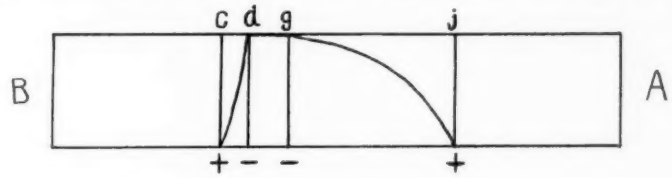
Continuation of accession soon results in approach of the wave toward p (the tip of the precordial electrode) through that region of the free wall of the left ventricle which lies subjacent to p. Obviously, the solid angle developed at p by the arbitrary subjacent wave rapidly becomes large in magnitude and positive in sign. Thus the usual, tall upstroke of R_4 results. This upstroke heralds the approach of the accession wave toward p as it passes outward through the ventricular wall. Moreover, the summit of R_4 signals the time of arrival of the wave at the subjacent epicardial surface. If, at this instant, the remainder of the ventricular muscle has been transgressed by the wave (not usually the case), the potential at p becomes zero and the downstroke of R_4 is recorded. Usually, the basal region of the free wall of the left ventricle is uninvaded at the instant specified, and a retreat of the wave in a direction away from p throughout the specified basal region results in a relatively small and negative solid angle. Thus, the downstroke of R_4 descends below the base line of the curve to form the descending limb of S_4. With invasion of the free wall of the left ventricle, accession of the ventricles is complete, and the solid angle and, consequently, the potential vanish. The ascending limb of S_4 is thus recorded.

In a like manner and for like reasons, the form of T_4 depends upon the order of regression locally in that region which is subjacent to p. If, in the subjacent region, the subepicardial elements of muscle commence regression ahead of the subendocardial units in the immediate neighborhood, the potential at p is positive; or, if the subsurface units (subepicardial and subendocardial) in the subjacent wall commence regression ahead of the remaining subsurface units, the potential at p is positive and T_4 is an upward movement. In children T_4 may be inverted normally, and it is assumed that subepicardial units of the subjacent ventricular wall undergo regression relatively late in comparison with neighboring units at the epicardial and endocardial surfaces. The order of regression of the muscle units between the subsurface units is immaterial.* The effective onset of regression ordinarily begins before QRS is complete, and, consequently, the so-called RS-T_4 junction of the curve is frequently displaced upward (in adults) through a small distance (= 0.1 or 0.2 millivolt).

Under normal circumstances, using V leads, the QRS complex is regularly introduced by an R deflection at positions 1, 2, and 3. In an

*See footnote page 781.

occasional instance the QRS complex may be comprised of a single QS deflection at position 1. The obvious explanation for the initially negative solid angle lies in the fact that an observer stationed at position 1 may, on looking through the base of the cone, observe the negative charge on the concave (retreating) surface of the accession shells S_R and S_L. The single QS deflection is encountered normally in the CF leads



(b)

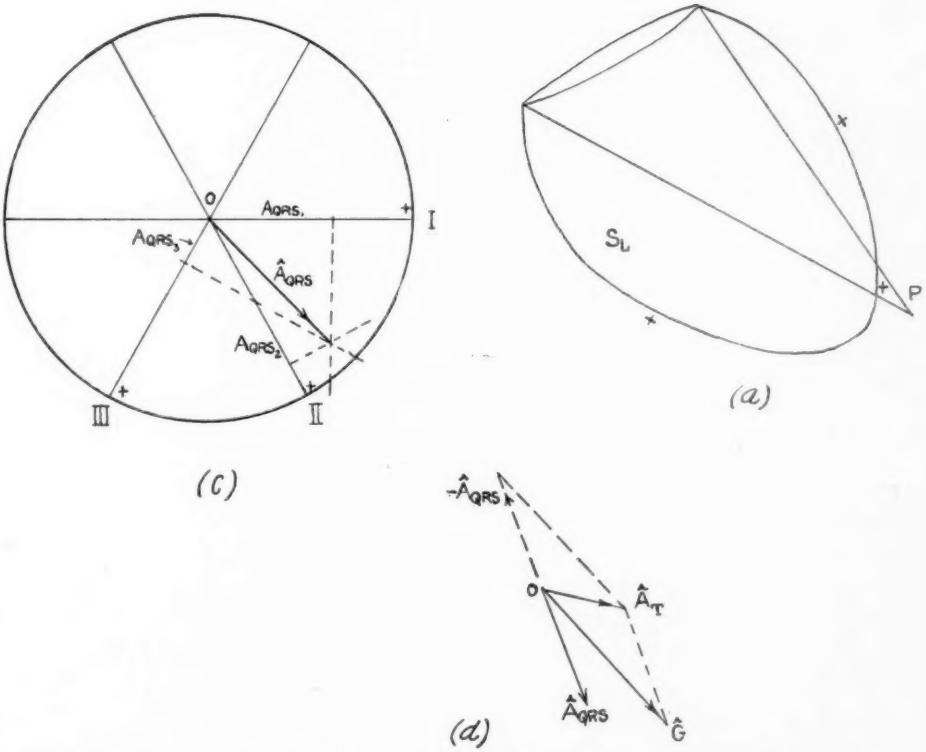


Fig. 5.—(*a*) Left ventricular accession shell S_L, with the proportional potential it produces at p, as measured by the solid angle subtended at p by the boundary of the shell. (*b*) Diagrammatic representation of the excitation wave cj at an instant during its passage along the muscle mass AB in the direction of B. (*c*) Showing the net areas A_{QRS_1}, A_{QRS_2}, and A_{QRS_3}, plotted out along the axes of the triaxial reference system. The relationship between these areas and the manifest mean axis $\hat{A}_{QRS}$ is likewise shown. (*d*) The geometric relationship of the manifest mean axes $\hat{A}_{QRS}$, $\hat{A}_T$, and $\hat{G}$. See text.

at positions 1 and 2. Here, the explanation is the same as that given for V leads, except that the leg potential (usually positive) favors the formation of the QS type of complex. Generally speaking, the amplitude of R of the precordial leads (semiunipolar and unipolar) normally increases from position 1 through position 4. At position 5 it may show a further increase (slight) or a decrease. At position 6 the amplitude of R is normally less than that encountered at position 5. The described sequence of normal variations is very important, inasmuch as limited damage in the subjacent ventricular wall may be recognized by a disturbance in the sequence, whereas one curve taken by itself is valueless.

We are now prepared to consider further the initial ventricular deflections of Fig. 4, *f*. Lead IVF shows that R has a rather broad upstroke which is probably not normal and which may possibly represent a low-grade, left-sided, intraventricular conduction defect. In this connection, a curve recorded from the patient shortly before death (not presented) showed complete heart block. The notch on the upstroke of S is part of the picture of right bundle branch block, or, to be more exact, is associated with the late aberrant spread of the accession wave into the right ventricle.

When recording curve A, Lead CF_2 was used. The minute R and the initial, sharp downstroke of QRS must represent accession of the left ventricle, for, in complete right bundle branch block, only the shell S_L exists throughout this period. Moreover, the effects under consideration may be said to represent, chiefly, accession of that part of the left ventricle which lies nearest to the exploring electrode; that is, effects of the anterior free wall of the left ventricle and the neighboring anterior region of the interventricular septum. The small R under discussion represents the approach in this region of a small area of wave in a direction toward the tip of the exploring electrode. The following, initial, sharp downstroke indicates that the electrode potential has suddenly become negative, an event which may be accounted for in the following way:

The shell S_L is, no doubt, intact (of unit density) at the time of the sharp downstroke (= 0.04 second after the onset of accession). Moreover, S_L undoubtedly has two large circular boundaries at this time, one which defines the normal area S_1 of reduced magnitude, and a second, abnormal area S_3 created by a large septal infarct. The solid angle subtended at the exploring electrode tip by the former boundary is positive when the latter boundary is supposedly absent. Likewise, the solid angle subtended at the same point by the latter boundary is negative when the former boundary is supposedly absent. Inasmuch as the actual potential at position 2 is given by the sum of the two solid angles multiplied by $(\phi_1 + \phi_2)$, the resulting negative sense of the potential is actually accounted for, provided only that the infarct is relatively

large. The subsequent sharp upstroke heralds the approach of the accession wave in the subjacent free wall of the right ventricle. It occurs late (0.06 to 0.07 second after the onset of QRS), as might be expected when the right main branch of the His bundle is blocked.[16] The final downstroke represents the retreat of the accession wave through the lateral free wall of the right ventricle.

Curve B (Fig. 4, *f*) was recorded with the exploring electrode in the fourth intercostal space just lateral to the left border of the heart; that is, over the anterior free wall of the left ventricle. Here, the detailed explanation of the QRS complex is the same as for the normal recording from this point, except that the slow upstroke of S is abnormal because of the delayed retreat of the accession wave in a direction away from the electrode tip toward the free wall of the right ventricle. The sharp upstroke of R confirms opinion derived from the extremity leads regarding the integrity of the anterolateral free wall of the left ventricle. We are as yet unable to interpret the abnormal final ventricular deflections.

SECTION IV

ON THE REGRESSION PROCESS AND THE MEAN ELECTRICAL AXES

The T or final ventricular deflection represents the electrical effect produced by spread of the regression process over the ventricular muscle. The onset of T in the various leads indicates the time at which the magnitude of the regression effect is sufficiently great to influence the completed record. For the extremity leads, this time may be considerably later than the time at which regression actually begins at some ventricular point.

There are certain striking differences in the form of T as compared with the form of QRS. Obviously, these differences represent certain differences in the characteristics of the regression wave, as compared with those of the accession wave.

Let us consider a graphic representation of the excitation wave, cj of Fig. 5, *b*, as the wave travels along the cylindrical mass AB of cardiac muscle. Stimulation has occurred at the end A, so that the wave cj is traveling, at the instant under consideration, away from A in the direction of B. The wave may be subdivided, for descriptive purposes, into three zones, cd, dg, and gj. Within the zones Bc and jA, which lie, respectively, before and behind the excitation wave, the muscle cells are in the resting electrical state. The zone cd represents the accession wave within which the cells are in the process of passing from the resting into the excited electrical state. The cells within this zone are said to be undergoing the initial reversal of polarization. The length of the zone cd is equal to $v_o t_o$, the product of the velocity v_o of the accession wave by the time t_o elapsing between the beginning and completion of accession at a given point. Within the zone dg the muscle cells are in the fully excited state; that is, the cells have undergone a change

(reversal) of polarization which is maximal for the present excitation. The actual length or duration of the excited state is determined by the time after accession at which regression begins. The effective length or duration of the excited state depends upon the time after accession at which effective regression begins. The former duration, unlike the latter, is independent of the rate of regression at a point. In so far as the completed record is concerned, an increased rate of regression at a point may shorten the effective duration, whereas the actual duration may remain unchanged. The zone gj represents the regression wave within which the muscle cells are in the process of passing back from the excited into the resting electrical state. The cells within the zone designated are undergoing a second reversal of polarization. The length of the zone gj, or the length of the regression wave, is equal to $v_o t_1$, which is the product of the velocity v_o of the regression wave by the time t_1 that elapses between the beginning and completion of regression at a point.

In Fig. 5, *b*, the slope of the curve within the zone ed and the slope of the curve within the zone gj represent the respective rates of the initial and the final reversal of polarization at a point. Presumably, each curve is of exponential form. It is observed that the rate of the initial reversal is greater than the rate of the final reversal. Throughout the zone dg, no change of polarization occurs, and the curve representing the rate of change has no slope or is horizontal. Clearly, the curve within the zone ed appears to be nearly straight in comparison with the curve within the zone gj; this difference is caused by the more rapid rate of change of polarization in the former as compared with the slow rate of change in the latter. The assumption that the electrical moment $(\phi_1 + \phi_2)$ of the accession wave is constant is equivalent to the assumption that the length of the wave is very short, or that the initial reversal of polarization is, for all practical purposes, instantaneous.

Because of the tendency toward uniformity of physiologic activity by the various units of cardiac muscle, the order of accession tends to determine the order of regression. However, a local variation of this uniformity may alter locally the effective duration of the excited state, and, by so doing, alter the order of regression without affecting the order of accession.

The order of ventricular accession tends to determine the order of ventricular regression. The former determines the form of QRS, whereas the latter determines the form of T. Consequently, the form of QRS tends to determine the form of T. However, if there should occur a local variation in the uniformity of the effective duration of the excited state, the order of regression will not be the same as the order of accession, and the form of T will be altered by the local variation in effective duration of the excited state.

It is clear that, if the characteristics of the two waves, accession and regression, were identical except for polarity, and if the order of ven-

tricular accession determined completely the order of ventricular regression, and if the effects of accession were complete before those of regression commenced, the accession deflections (QRS) would be followed by regression deflections (T) of identical form except that the polarity of the corresponding deflections would be of unlike sign, one positive and the other negative.

Under normal circumstances, the resting states before and after a given excitation are comparable. Consequently, the total change of polarization produced during accession is comparable to the total change of polarization produced during regression. Any difference encountered, other than polarity, in the total effect produced during accession as compared with the total effect produced during regression may be ascribed, therefore, to a difference in the order of regression as compared with the order of accession. The area under the curve of QRS is equal to the product of the mean accession voltage by the duration of QRS, and is a measure of the total electrical effect produced by ventricular accession.[17] Likewise, the area under the curve of T is equal to the product of the mean regression voltage by the duration of T, and is a measure of the total electrical effect produced by ventricular regression. Let us denote the area under QRS by A_{QRS_1} and the area under T_1 by A_{T_1}. Inasmuch as the ordinate under the curve is measured in microvolts and the duration in seconds, the areas A_{QRS_1} and A_{T_1} are measured in microvolt-seconds (= m.v.s.). According to the notation adopted for Lead I, the areas under QRS_2 and T_2 are denoted by A_{QRS_2} and A_{T_2}, respectively, and similar notation holds for Lead III. In general, an area of the kind under consideration has a sense, positive or negative, depending on whether the net area under the subdivision of the curve considered measures positive or negative.

If the numerical values of any two of the quantities A_{QRS_1}, A_{QRS_2}, and A_{QRS_3} are plotted out on the proper half of the corresponding reference axis, commencing at the origin O (see Fig. 5, *c*), they determine a vector quantity $\hat{A}_{QRS}$, of which each is a projection. The origin of $\hat{A}_{QRS}$ is at O, and the terminus of $\hat{A}_{QRS}$ is at the intersection of two perpendiculars drawn to the outward extremities of the plotted areas.

In so far as the triaxial reference plane is concerned, the magnitude of $\hat{A}_{QRS}$ is a measure of the total electrical effect produced by ventricular accession, and the direction of $\hat{A}_{QRS}$ is the direction in which the accession wave travels over the average element of ventricular muscle.

A vector quantity $\hat{A}_T$ is determined from any two of the areas A_{T_1}, A_{T_2}, and A_{T_3} in essentially the same manner used for determining $\hat{A}_{QRS}$. The magnitude of $\hat{A}_T$ is a measure of the total electrical effect produced by ventricular regression, and the direction of $\hat{A}_T$ is the inverse direction in which the regression wave travels over the average element of ventricular muscle. Thus, if the order of ventricular accession determined

completely the order of ventricular regression, so that the course of the two waves was the same, we would have the relation

(4-1) . . . $\hat{A}_{QRS} = -\hat{A}_T$,

and the sum of the two vectors is zero. Inasmuch as relation (4-1) does not hold for the normal human electrocardiogram, it is clear that, even under normal circumstances, the order of ventricular regression is not the same as the order of ventricular accession. Consequently, there is a normal lack of uniformity in the effective duration of the excited state in various parts of the ventricular muscle at the epicardial and endocardial surfaces. The duration of the excited state in muscle layers between the subsurface layers is immaterial.* The sum of the vectors $\hat{A}_{QRS}$ and $\hat{A}_T$ gives a new vector, $\hat{A}_{QRST}$, or $\hat{G}$, which is a measure of the lack of uniformity in the effective duration of the excited state in various parts of the subepicardial and subendocardial muscle layers. In so far as the frontal plane of the body is concerned, the magnitude of $\hat{G}$ is a measure of the total effect produced by the lack of uniformity in the effective duration of the excited state, whereas the direction of $\hat{G}$ is that of a line along which the variations in the effective duration of the excited state are greatest.

The vectors $\hat{A}_{QRS}$ and $\hat{A}_T$ are known, respectively, as the manifest mean electrical axis of accession and the manifest mean electrical axis of regression. The vector $\hat{G}$ is known as the manifest mean electrical axis of QRST, or as the gradient, which may be said to point toward regions in the ventricular muscle at the epicardial and endocardial surfaces in which the average duration of the excited state is greatest, towards regions in the muscle at these surfaces where the average duration is least.

Inasmuch as the vectors $\hat{A}_{QRS}$, $\hat{A}_T$, and $\hat{G}$ are determined from measurements made on the extremity leads, the vectors are restricted to the plane of the triaxial reference system. It is clear, however, that the electrical forces in the ventricles are not thus restricted, and must have a set of three mean axes operating in three-dimensional space. In order to avoid confusion, the set of spatial mean axes are denoted $S\hat{A}_{QRS}$, $S\hat{A}_T$, and $S\hat{G}$, where the prefix S merely indicates three-dimensional space. Any one of the manifest mean axes is simply the projection of the corresponding spatial mean axis upon the plane of the triaxial reference system. For the relations connecting the three axes of both sets, spatial and manifest, we have

(4-2) . . . $S\hat{A}_{QRS} + S\hat{A}_T = S\hat{G}$,

and

(4-3) . . . $\hat{A}_{QRS} + \hat{A}_T = \hat{G}$,

respectively. At the present time our knowledge of the spatial mean

*See footnote, page 781.

axes must depend upon speculation based upon the known activities of their projections, the manifest mean axes. Nevertheless, the definitions herein offered for the manifest mean axes[17] apply equally well to the spatial mean axes.

The triaxial reference system, which has been found useful in dealing with the instantaneous axis, is likewise useful in dealing with the manifest mean axes. Moreover, the triaxial reference system may be expanded into a tetraxial reference system for dealing with the spatial mean axes, i.e., let a z-axis pass through the origin O, normal to the triaxial reference plane, and, according to custom, let the positive half of the z-axis lie dorsal, and the negative half ventral, to the triaxial reference plane.

The discussion which follows will deal only with the manifest mean axes $\hat{A}_{QRS}$, $\hat{A}_T$, and $\hat{G}$. We may write eqn(4-3) in the form

$$\hat{A}_T = -\hat{A}_{QRS} + \hat{G}, \qquad (4\text{-}4)\ldots$$

which states that the mean axis of T is equal to the sum of two vectors, the inverse of the mean axis of QRS and the ventricular gradient. The relation clearly shows that the area under T depends upon two components, the area under QRS and the ventricular gradient. Any factor which alters the area under QRS will, by so doing, alter the area under T secondarily. Changes in T caused by changes in QRS are called secondary T-wave changes.[17] On the other hand, any factor which alters the ventricular gradient will, by so doing, alter the form of T primarily without altering the form of QRS. Changes in T caused by alterations of the gradient are known as primary T-wave changes. In electrocardiographic interpretation it is a matter of great clinical importance to ascertain which T-wave changes are primary, secondary, or a combination of both.

For a geometrical interpretation of eqn(4-4), we may consult Fig. 5, *d*. Clearly, $\hat{A}_T$ is the directed diagonal of a parallelogram of which $-\hat{A}_{QRS}$ and $\hat{G}$ form two sides. It is to be recalled that all of the origins of the manifest mean axes coincide with the origin O of the triaxial reference system (not shown). Under most normal circumstances, the mean axes lie in the region defined by the sixth and the adjacent halves of the fifth and first sextants. The plotted points in Fig. 6 indicate the positions of the termini of 100 gradients as ascertained by measurement of electrocardiograms from as many normal adults. In each of the 100 normal adults, $\hat{G}$ was found to lie nearly collinear with $\hat{H}$, the base-apex axis of the ventricles. The axis $\hat{H}$ was ascertained directly from the subject's chest roentgenogram.*

A further consideration of Fig. 5, *d* shows that, if the terminus of $\hat{A}_{QRS}$ is made to describe any arbitrary path whatever about O, while the gradient remains fixed, the terminus of $\hat{A}_T$ describes a path of similar form about the terminus of $\hat{G}$. The second path, however, appears as if rotated through 180 degrees (when compared with the first), and

*Dr. R. H. Bayley, Dr. J. E. Holoubek, and Dr. A. B. Holoubek were co-workers in the preparation of these data (1940).

can thus be made to describe all possible variations of the area under T_1, T_2, and T_3 due to all possible variations of the area under QRS. In a like manner, if the terminus of $\hat{G}$ is made to describe any arbitrary path whatever about O while $\hat{A}_{QRS}$ remains fixed, the terminus of $\hat{A}_T$ describes an altogether similar path about the terminus of $-\hat{A}_{QRS}$. The second path can thus be made to describe all possible variations in the area under T_1, T_2, and T_3 due to all possible variations of the gradient. All possible secondary and primary changes, respectively, in the area under T may, in this manner, be arbitrarily obtained.

Assuming that the gradient is normal, the position of $\hat{A}_{QRS}$ which gives the maximal negative area under T_1 is such that $\hat{A}_{QRS}$ coincides with the positive half of the RL-axis. Under the circumstances, the net areas under QRS_2 and QRS_3 are equal in magnitude and unlike in sign; the former is positive and the latter negative. Again assuming that the gradient is normal, the position of $\hat{A}_{QRS}$ which gives the maximal negative area under T_3 is such that $\hat{A}_{QRS}$ coincides with the positive half of the LF-axis. Under the circumstances, the net areas under QRS_1 and QRS_2 are equal in magnitude and unlike in sign; the former is negative and the latter positive.

It has been herein pointed out that, within relatively narrow limits, the normal gradient $\hat{G}$ is fixed with respect to $\hat{H}$. Inasmuch as the position of $\hat{H}$ varies normally in one subject as compared with another, it is clear that the normal position of $\hat{G}$ must likewise vary. It is also clear that the precise position of $\hat{G}$ with respect to the triaxial reference system is of great importance in ascertaining whether the areas under T_1 or T_3 will be less positive or actually negative for the described critical positions of $\hat{A}_{QRS}$.

To illustrate, let us suppose that Subject A, with a vertical heart, has a normal gradient that lies in that half of the fifth sextant which is adjacent to the sixth. In addition, let us suppose that Subject B, with a horizontal heart, has a normal gradient at 3 o'clock, or collinear with the positive RL-axis. Let us further suppose that $\hat{A}_{QRS}$ for both subjects is like in magnitude and lies at 3 o'clock. Furthermore, the appearance of QRS in both subjects is similar. In Subject A the situation is abnormal, for $\hat{A}_{QRS}$ makes a polar angle of more than 60 degrees with respect to $\hat{H}$ or $\hat{G}$ (the maximal normal is about 30 degrees, Fig. 6). The abnormality of QRS is evidenced by the positive rotation (counterclockwise) with respect to $\hat{H}$ or $\hat{G}$, and may be ascribed to preponderant hypertrophy of the left ventricle. Under the circumstances, T_1 is inverted and T_2 is low or diphasic. Moreover, the T-wave changes are secondary and add nothing further to the diagnosis. In Subject B the entire situation is within the range of normal. T_1 is necessarily a positive deflection unless the magnitude of $\hat{A}_{QRS}$ actually exceeds that of $\hat{G}$. Since $\hat{G}$ was assumed to be normal, the abnormality of $\hat{A}_{QRS}$ must (in the event that T_1 is inverted) consist of an abnormal growth of A_{QRS} without rotation. A growth of A_{QRS} may result from ventricular hyper-

trophy. Therefore, in the event that A_{QRS} exceeds G, with consequential inversion of T_1, the T-wave changes are secondary in kind, and add nothing further to the diagnosis of ventricular hypertrophy for Subject B.

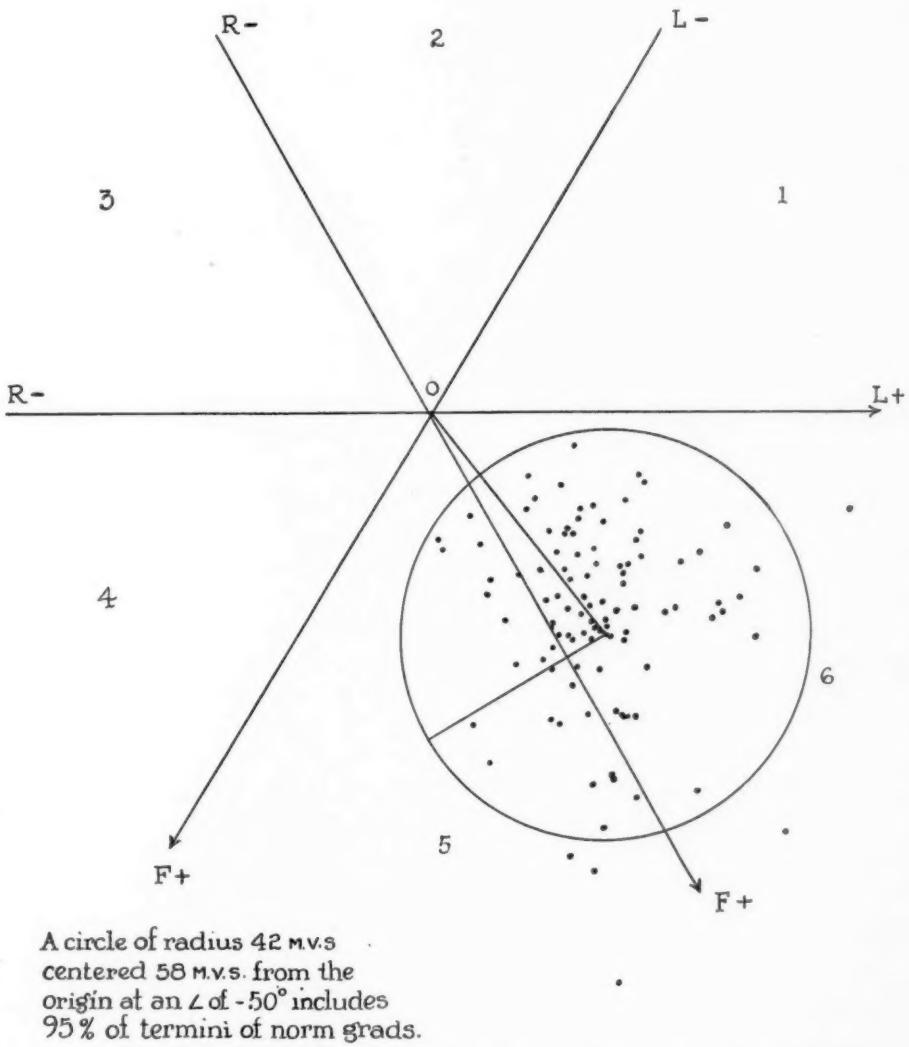


Fig. 6.—Illustrating the relationship with respect to the triaxial reference system of 100 points. Each point indicates the position of the terminus of G, as measured from a presumably normal electrocardiogram recorded from an adult subject with no clinical evidence of heart disease. (Bayley, R. H., Holoubek, J. E., and Holoubek, A. B., 1940.) See text.

Let us again consider Subject A. The vector $\hat{H}$ lies in that half of the fifth sextant which is adjacent to the sixth. Let us now suppose that both $\hat{A}_{QRS}$ and $\hat{G}$ are found to lie along the positive axis of RL, and that the magnitude of $\hat{G}$ is one-third greater than that of $\hat{A}_{QRS}$. Here, T_1 and T_2 are positive and T_3 is inverted. So far as the T waves are alone concerned, they appear to be normal. Actually, however, a decided abnormality is present. In the first place, $\hat{A}_{QRS}$ shows the same abnormality (a rotation) as previously described, and the interpretation is the same. In the second place, the apparently normal T waves are actually abnormal because of the presence of secondary changes which have been annulled by primary changes. The latter are evidenced by a growth and positive rotation of $\hat{G}$ with respect to $\hat{H}$. The interpretation of the gradient growth and rotation will not be considered at this point. However, had not the positions of $\hat{A}_{QRS}$ and $\hat{G}$ been considered with respect to $\hat{H}$, the anatomic axis of the ventricles, a diagnosis of a normal electrocardiogram might have been made, as in the case of Subject B.

When the area under a T deflection is small, the deflection is either low or diphasic. When the area under T is zero, the deflection may not exist, or it may be diphasic or even triphasic.

It may be noted that the term "axis deviation" has thus far been avoided. In my opinion, the current use of the term is more harmful than helpful. A so-called axis based upon the amplitudes of the QRS deflections and expressed as deviated with respect to the triaxial reference system can have little or no accurate interpretative value. The three manifest mean axes $\hat{A}_{QRS}$, $\hat{A}_T$, and $\hat{G}$ are of equally great importance, and must be described in direction and magnitude, both with respect to the triaxial reference system and with respect to the base-apex axis $\hat{H}$. Moreover, "deviation" of a mean axis may be one of direction and magnitude, singly or in combination, away from or toward, an expected normal position. The terms adopted here are "diversion," indicating a change away from the normal in magnitude and direction, singly or in combination, and "reversion," indicating a change toward the normal in magnitude and direction, singly or in combination. In the event of diversion or reversion, it is necessary to state the specific axis with respect to which the diversion or reversion has taken place. Depending upon the circumstances, it may be found most convenient to change from one axis of reference to another. In the foregoing example of Subject A, the mean axis abnormality is most conveniently described (in the first instance) as a positive diversion of $\hat{A}_{QRS}$ with respect to $\hat{H}$, and (in the second instance) as a positive diversion of $\hat{A}_{QRS}$ and $\hat{G}$ with respect to $\hat{H}$.

All of the polar angles which the various mean axes and reference axes make with respect to one another are subtended at the origin O of the triaxial reference system, and are described as positive or nega-

tive, depending upon whether the direction of measurement appears counterclockwise or clockwise, respectively. The term "rotation" of a mean axis implies a change of direction only, and the direction of rotation is positive or negative, depending on whether its motion appears counterclockwise or clockwise to an observer looking toward the frontal plane from a point anterior to the plane.

SECTION V

ON PRIMARY T-WAVE CHANGES

As described in the previous section, all primary T-wave changes are caused by a local alteration in the normal lack of uniformity of duration of the excited state in the subepicardial and subendocardial muscle layers of the ventricles. At the present time no understanding has been reached regarding the fundamental reason for the normal lack of uniformity of the effective duration of the excited state. It is clear, nevertheless, that the lack of uniformity in question is local, and exists at the epicardial and endocardial surfaces of the ventricular muscle. Moreover, the duration of the excited state in muscle units between the surface layers is immaterial. The normal ventricular gradient has a base-apex direction,[17] and is said to point away from regions of the subepicardial and subendocardial muscle layers in which the average duration of the excited state is greatest, toward regions at these surfaces where the average duration is least. Consequently, the normal gradient may mean that the average duration of the excited state is greatest in the subepicardial, as compared with the subendocardial, muscle; it may mean a greater average duration of the excited state in the basal, as compared with the apical, muscle units subjacent to the ventricular surfaces; or, it may mean a combination of these possibilities. Certain phenomena concerned with the motions of the normal manifest mean axes have led some investigators[18] to believe that the spatial gradient $S\hat{G}$ has a posterior as well as an apical direction. If this opinion is correct, the spatial gradient may mean that the average duration of the excited state is greater in the surface muscle units of the anterobasal regions, as compared with the posteroapical regions of the ventricular walls. It is likewise clear that, until more is known about the factor or factors which account for the normal ventricular gradient, little progress can be expected concerning the fundamentals of the abnormal gradient.

In view of the foregoing statements, it might be concluded that little of practical clinical value is to be found in the present discussion. Such is emphatically not the case. There are a number of varieties of factors which are known to operate clinically in such a manner as to alter the normal gradient and thus bring about primary T-wave changes. Often it is a difficult matter for the clinician to decide which factor or group of factors is operating to produce the particular primary T-wave changes under consideration. When more than one factor is known to be present,

attempts can be made to remove one factor at a time during a careful study of the concurrent serial electrocardiograms. In this rather tedious manner, reliable decisions can be reached regarding the interpretation to be placed upon many of the primary T-wave changes. Routine interpretations of primary T-wave changes are to be made, therefore, with great caution.

Among the factors which may alter the gradient singly or in combination are variations of the blood hydrogen ion concentration, various hormones, temperature, anemia, toxic agents, drugs of various kinds (digitalis, in particular), and local ventricular ischemia. Only the last of these factors is considered in the discussion which follows.

In general, there appear to be two important kinds of local ventricular ischemia, acute and chronic. Evidence of either kind may be present in the electrocardiograms from a subject who has no cardiac pain. On the other hand, a history of cardiac pain is characteristically present in subjects whose electrocardiograms display evidence of acute local ventricular ischemia. Subjects whose electrocardiograms display evidence of chronic local ventricular ischemia frequently give a history of recurrent attacks of paroxysmal dyspnea. The electrocardiographic changes ascribed to acute local ventricular ischemia do not differ materially in kind from those ascribed to the chronic form of local ventricular ischemia. In fact, the only significant differences are the rate of appearance, the duration, and the rate of disappearance of the T-wave changes. In the acute variety, the appearance is usually a matter of minutes, hours, or a few days; the duration is usually a matter of minutes, days, or a few weeks at the most; and the rate of disappearance is comparable to the rate of appearance. In the chronic variety, the appearance is a matter of a few or many months; the duration is a matter of many months or a number of years; and the disappearance is often interrupted by death. It is known that the acute variety may be evidenced electrocardiographically for as long as two weeks in man, without the involved muscle showing any gross or microscopic abnormalities.[19] The chronic variety may indicate a concurrent development of myocardial fibrosis. In both varieties of local ventricular ischemia, the associated varieties of heart disease are hypertensive, syphilitic, and arteriosclerotic, singly or in combination. The acute variety is most commonly encountered in the arteriosclerotic type of heart disease. There can be little doubt that spasm of a subdivision of the coronary arterial tree is at least a precipitating factor in many of the instances of acute or transitory local ventricular ischemia. A somewhat subacute form frequently develops and disappears concurrently with the transitory hypertension of acute nephritis. Here, the electrocardiographic evidence is, strangely enough, of a kind strikingly similar to the chronic variety associated with chronic hypertension. Moreover, if the evidence in either instance may be interpreted as indicating local ischemia, it indicates, more strangely still, a local involvement of the

muscle ordinarily irrigated by the left coronary artery (see following analytical explanation).

The precise location and the intensity of the ischemia are the chief factors which determine the kind and magnitude of the associated T-wave changes. These primary T-wave changes are caused by a local prolongation of the average duration of the excited state in the neighboring surface muscle layers. Consequently, local ischemia which is confined to muscle between the surface layers is without associated electrocardiographic changes.

The muscle layer subjacent to the endocardial surface differs in two important respects from the layer subjacent to the epicardial surface. The former is nourished by a comparatively rich arterial plexus.[20] Moreover, when the local intravascular pressure falls because of impaired coronary flow, the subendocardial muscle layer is irrigated by blood from the ventricular cavity, i.e., blood which flows through the thebesian veins. It is conceivable that the innermost layer of muscle cells may obtain adequate nourishment by direct imbibition across the endocardium. It is clear, therefore, that, as a large zone of local ventricular ischemia develops and reaches transmural proportions, the intensity of the ischemia tends to be greater in the subjacent epicardial, than in the subjacent endocardial, muscle. Because of the lamellar character of the regression wave, the measured degree of the local ischemia is proportional to the difference between the degree of the local ischemia at the epicardial and that at the endocardial surface. With the development of local ischemia, the gradient undergoes a diversion which tends to bring the direction of the vector $S\hat{G}$ into that of a line drawn from the center of the local ischemia toward the center of the involved ventricle. Generally, then, if local ischemia involves that portion of the ventricular muscle which is ordinarily irrigated by the right coronary artery, the manifest gradient $\hat{G}$ sweeps through a positive rotation[19] into the first, or the neighboring half of the second, sextant. Let us assume that $\hat{A}_{QRS}$ retains its normal position in the sixth sextant (Fig. 7, *a*). The vector $\hat{A}_T$, when altered by the described diversion of $\hat{G}$, is now such as to measure a small positive or zero area under T_1, and equally large negative areas under T_2 and T_3. If the local ischemia involves that portion of the ventricular muscle which is ordinarily irrigated by the left coronary artery, the manifest gradient $\hat{G}$ sweeps through a negative rotation into the fifth or the adjacent half of the fourth, sextant.[19] Let us again assume that $\hat{A}_{QRS}$ retains its normal position in the sixth sextant (Fig. 7, *b*). The vector $\hat{A}_T$, as altered by the described diversion of $\hat{G}$, is now in a position which measures a large negative area under T_1, an equally large positive area under T_3, and a zero or nearly zero area under T_2. When the areas under the T waves are large (positive or negative), the effective events of regression may begin before those of accession are complete, and the RS-T junction is

displaced from the base line of the curve in the direction of the regression effect. RS-T junction displacements of this kind are not to be confused with those ascribed to injury (see next section).

In so far as the general form of the T wave is concerned, there are no important differences between those changes ascribed to uncomplicated local ischemia and those ascribed to the perifocal ischemia of infarct. As a matter of fact, the acute variety of the former changes occasionally heralds ventricular infarction, and the primary T-wave changes diasppear temporarily as a result of the development of injury effects. Subsequently, the same T-wave changes reappear subtotally as evidence of the perifocal ischemia of infarct. The injury effects (RS-T junction displacements) concurrently vanish with the reappearance of local ischemia effects. An example of the final appearance and disappearance of the changes ascribed to the perifocal ischemia of infarct is shown in Fig. 7, *c*. The associated path traced out by the terminus of the manifest gradient $\hat{G}$ is shown in Fig. 7, *d*.

In the semiunipolar and unipolar leads, the relative delay of regression at the epicardial surface subjacent to the exploring electrode is evidenced by a sharp inversion of the T deflection. With anterolateral ischemia, this effect may be shown in curves recorded at the fourth, fifth, and sixth precordial positions.

Strictly apical ischemia at first shortens the gradient, and, if sufficiently intense, may reverse it into the third sextant. The former gradient change tends to reduce the positive areas under the normally upright T deflections, whereas the latter change may account for sharp inversion of T_1, T_2, and T_3, together with inversion of T at the fourth precordial position. During the development of a gradient reversal of this kind, T_1, T_2, and T_3 become inverted before the actual gradient reversal occurs. If $\hat{A}_{QRS}$ and $\hat{G}$ are collinear in the sixth sextant, $\hat{A}_T$ appears in the third sextant as the magnitude of $\hat{G}$ becomes less than that of $\hat{A}_{QRS}$.

Finally, it is conceivable that a diffuse ischemia, localized to the basal regions of the ventricular walls, might produce an excessive increase in the magnitude of the normal gradient without altering its normal direction. The normally positive areas under T_1 and T_2 would be increased accordingly. In one instance of this kind the magnitude of the gradient measured 160 m.v.s. The curve appeared essentially normal in all other respects. The patient had had typical attacks of cardiac angina throughout the month which preceded the recording. For an example of electrocardiographic changes ascribed to local ischemia, see Fig. 8, *a* and *b*.

The problem of local ventricular ischemia, as depicted in this section, is incomplete to the extent that injury and blocking effects, which are ascribed to a second and more severe grade of impaired blood supply, have not been dealt with (see next section).

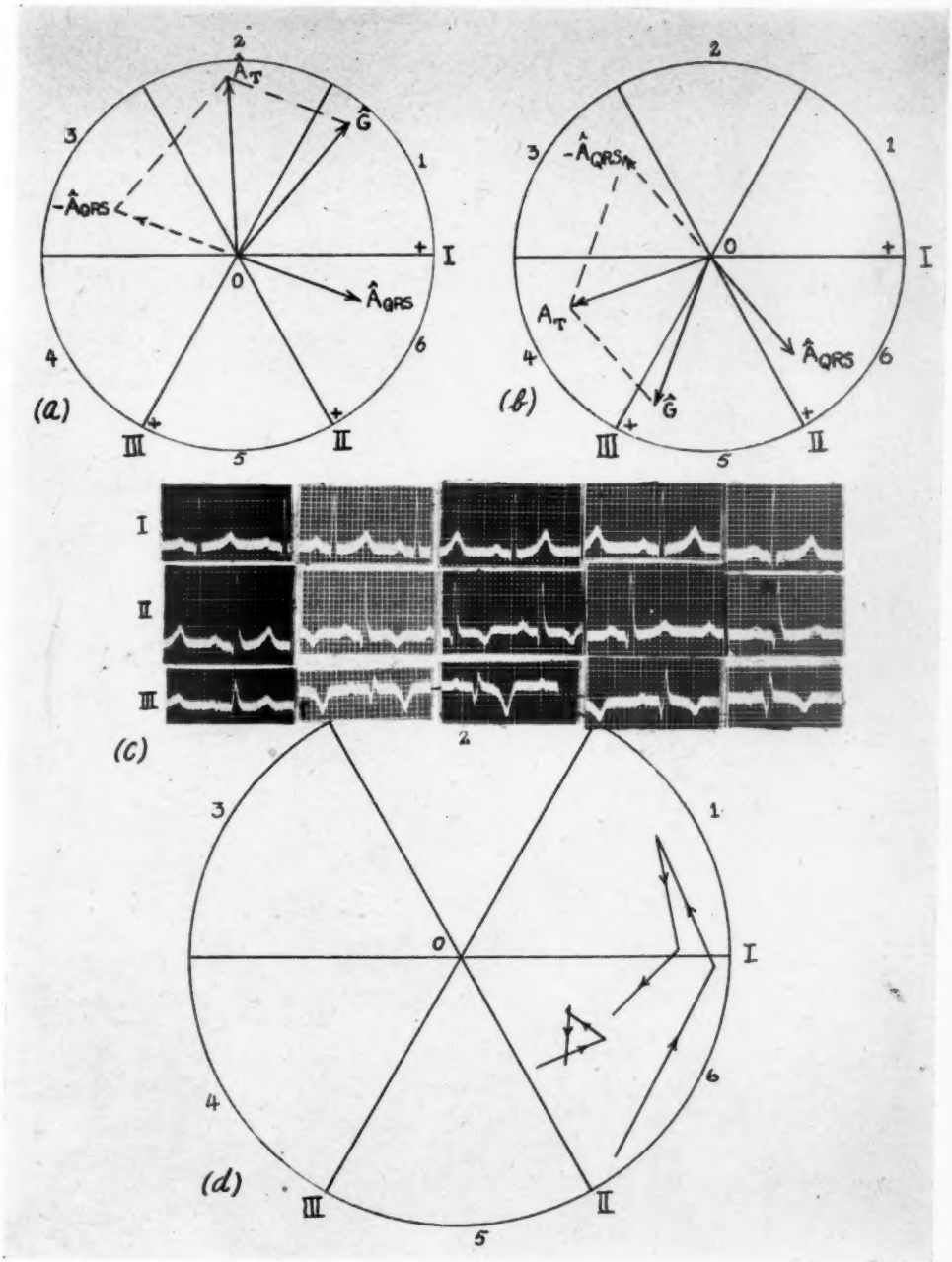


Fig. 7.—(*a*) Showing the manifest mean axes in the positions considered characteristic of local ventricular ischemia of the muscle that is ordinarily irrigated by the right coronary artery. (*b*) Showing the manifest mean axes in the positions considered characteristic of local ventricular ischemia of the muscle which is ordinarily irrigated by the left coronary artery. (*c*) Five serial electrocardiograms recorded over a forty-day period from a subject who had had recent posterior infarction. The left-hand curve was recorded before, and the remaining curves after, infarction. QRS is of the $R_1Q_2Q_3$ variety. Note the appearance and disappearance of primary T-wave changes ascribed to the zone of perifocal ischemia. (*d*) The path restricted to the sixth sextant is that described by the terminus of $\hat{A}_{QRS}$ throughout the forty-day period over which the serial curves in (*c*) were recorded. The path restricted to the sixth and first sextants is that traced out by the terminus of G as the gradient undergoes the final diversion and subsequent reversion during the same forty-day period. See text.

SECTION VI

ON THE INJURY EFFECT AND ITS RELATIONSHIP TO MYOCARDIAL INFARCTION

According to the notation hereinbefore adopted, the ventricular regression effect "writes" the T sÊ-loop of the three-dimensional vectorcardiogram, and the T Ê-loop of the two-dimensional vectorcardiogram. The latter is the projection of the former upon the plane of the triaxial reference system. Moreover, the T sÊ-loop is the path described in space by the terminus of sÊ, the instantaneous axis of regression. The relationship between these loops and the T deflections of the extremity leads is the same as that previously described as connecting the QRS loops with the initial ventricular deflections of the extremity leads. Regression of the auricles also produces a measurable effect in the vectorcardiogram and in the extremity leads, but the effect is ordinarily obscured by the deflections of ventricular accession.

In man, the RS-T junction, as seen in the precordial leads, is often displaced upward normally from the base line for a distance of one or two millimeters, indicating that a regression effect has already commenced at the time at which accession terminates. For the most part, however, the regression effect does not manifest itself in the extremity leads until the lapse of a variable short interval of time after accession terminates. This interval constitutes the so-called RS-T segment, which is written on or nearly on the base line of the curve.

It is clear that the onset of T in the extremity leads does not represent the onset of ventricular regression, but merely the time at which the magnitude of the regression effect is sufficiently great to affect the completed record. Under certain circumstances the magnitude of early regression is sufficiently great to affect the completed record at the time at which ventricular accession ends. Whenever this is the case, the RS-T segment is absent, and the onset of T appears to take off from the final ascending or descending limb of QRS. In reference to this event, the RS-T junction is said to be displaced above or below the base line. If the duration of QRS is prolonged (as in bundle branch block), the RS-T segment is characteristically absent and the junction is often displaced. Early regression and prolonged accession are likely to occur together in effecting an RS-T junction displacement. Junction displacements caused by these factors operating singly or in combination are referred to as displacements of the permanent type, in contrast to a temporary variety which is associated with the injury phenomenon of ventricular muscle. The permanent variety may ordinarily be recognized by its association with QRS complexes which have large areas under the curve, and by the fact that the direction of the displacement is like in sign to that of the area under T, the adjacent deflection.

It is the purpose of the present discussion to deal with the temporary variety of RS-T junction displacement which is associated with injury

of ventricular muscle. The term injured muscle, as used throughout the discussion, implies an altered physiologic, rather than an altered structural, change. The alteration is recognized by the associated electrocardiographic changes, which, in a given case, may or may not prognosticate detectable structural change. As ordinarily observed in connection with disease of the coronary arteries, the zone of injured muscle is ischemic in the sense that its blood supply is insufficient, and, except for the degree of this insufficiency and the electrical effects produced, it resembles a zone of local ischemia, as described in Section V. The injured zone is regarded as a second and more severe grade of local ischemia. Obviously, the two grades are closely related, and, depending upon the circumstances, one grade may pass into the other. In a given curve, almost any combination of the associated effects may be encountered.

In Section V, a zone of local ischemia was described as characterized by a local prolongation in the effective duration of the excited state, or by a local, tardy onset of regression. The next grade of impaired function quite naturally appears to be an inability to complete locally the delayed regression process. In terms of the membrane theory, a subnormal regression process of this kind constitutes a tardy subnormal change of polarization on regression throughout the injured zone. In general, the electrical effects which are produced depend upon the location of the injured zone with respect to the ventricles as a whole, upon the distribution of the injured zone with respect to the epicardial and the endocardial surfaces, and upon the degree of subnormality of the change of polarization throughout the injured zone.

ON THE EFFECTS OF AN INJURED LAMINA

The experimentally injured region of the epicardial surface of the ventricles, or the region of local or diffuse pericarditis takes the form of a thin, shell-like lamina of injured cells at the periphery of the damaged area. The lamina separates the damaged region from the surrounding normal muscle. Because of the subnormal change of polarization which occurs on regression of the injured lamina, there exists, during diastole, a gradient in the intensity of polarization throughout the injured lamina. In any element of the lamina, the direction of gradient increase is perpendicular to the surfaces of the injured element in a direction away from the damaged toward the normal muscle. Consequently the injured lamina acts electrically, during diastole, like a steady double-layer, with its source surface adjacent to normal, and its sink surface adjacent to damaged, muscle.[15] Familiarity with the considerations advanced in Sections I and II concerning the character of the field produced by an electrical double-layer enables the immediate formation of an expression which describes the potential V_i' at any point p in the conductor near the injured region. We have

(6-1) ... $$V_i' = \phi_i' \, \Omega_i$$

where ϕ_i' is the electrical moment during diastole of the injured lamina, and depends upon the difference of the intensity of polarization at the two lamellar surfaces, one adjacent to the damaged, and the other adjacent to the normal, muscle; and where Ω_i is the solid angle subtended at p by the boundary of the injured lamina. Unless the damaged region extends entirely through the ventricular wall, as might be the case for a stab wound, the boundary of the injured lamina resides at the epicardial surface. Moreover, Ω_i is positive or negative (during diastole), depending on whether an observer stationed at p, and looking through the cone, views the injured lamina through *normal* or through *damaged* muscle.

Let us now examine the potential at p during systole or during the excited ventricular state. Accession constitutes the initial reversal of polarization; consequently, except for a new intensity of polarization at the surfaces of the injured lamina and the reversed polarity of the injured lamina, the source-sink distribution of the field of injury is unchanged during systole. Thus, if V_i'' denotes the injury potential at p during systole, and if ϕ_i'' denotes the electrical moment of the injured lamina during systole, we have

$$(6\text{-}2) \ldots \qquad V_i'' = \phi_i'' \Omega_i$$

where Ω_i is now positive or negative, depending on whether an observer stationed at p, and looking through the cone, views the injured lamina through *damaged* or through *normal* muscle. When the galvanometer is standardized during diastole a compensating current is introduced into the body-galvanometer circuit which neutralizes the effect during diastole of an injury current. Consequently, during systole, when the flow of injury current reverses, the compensating current is left free to flow around the circuit with the systolic injury current. The total effect on the completed record occurs, therefore, only during systole, and consists of the sum of two currents, one described by the right-hand side of eqn(6-1), with the sign changed, and the other described by the right-hand side of eqn(6-2). Consequently, the injury potential V_i at p, as depicted by the completed record, is given by

$$(6\text{-}3) \ldots \qquad V_i = (\phi_i' + \phi_i'')\Omega_i,$$

and if in this expression we define the content of the parentheses by ϕ_i, we have

$$(6\text{-}3) \ldots \qquad V_i = \phi_i \Omega_i$$

for use in the description of the injury potential produced at the tip of the exploring electrode by the presence of an injured lamina.

Relation (6-3) has a number of important and simple applications. In acute diffuse pericarditis, which damages the subepicardial muscle layer, the injured lamina has a free edge, or boundary, encircling the base of the ventricles, whereas the configuration of the outer surface

of the injured lamina is very nearly that of the ventricular epicardium itself. At all points within, or at, the surface of the conductor outside the heart, and on the inferior side of a plane passed through the boundary of the injured lamina, the injury potential is positive; at all points within, or at, the surface of the conductor on the other side of the plane, the injury potential is negative; at points within, or at, the surface of the conductor and within the specified plane outside the boundary of the injured lamina, the injury potential is zero; and, finally, at all points within the plane inside the boundary of the injured lamina, the injury potential is $-2\pi\phi_i$. Within the heart the injury potential is negative.

In dealing with the injured lamina in regard to its effect on the RS-T junctions of the extremity leads, we are at liberty to construct during systole the spatial axis of injury $s\hat{E}_i$, and its projection $\hat{E}_i$, upon the plane of the triaxial reference system in a manner similar to that used in dealing with the spatial and manifest axes of accession. Thus $s\hat{E}_i$ is given by the relation

$$(6\text{-}4)\ldots \qquad s\hat{E}_i = S_i\hat{e}_i$$

where S_i is the plane area circumscribed by the boundary of the injured lamina, and polarized in the same sense as the injured lamina is polarized during systole, and where $\hat{e}_i$ is a unit vector in the direction of the outward-drawn normal to the positive surface of S_i. Relation (6-4) shows that the magnitude of the vector $s\hat{E}_i$ is equal in units of length to the area of S_i in units of area, and is, moreover, independent of the configuration of the surfaces of the injured lamina. In the case of acute diffuse pericarditis, S_i lies at the ventricular base, with its positive surface directed toward the ventricular apex. Consequently, $s\hat{E}_i$ is collinear with the anatomic axis $\hat{H}$, and the vector $\hat{E}_i$ splits the sixth sextant. Clearly, the measured injury potential is a concordant positive displacement of the RS-T junctions of all extremity leads, large in Lead II, intermediate in Lead I, and small or zero in Lead III. It may be observed further that a local pericarditis which caps the ventricular apex produces the same, or nearly the same, effects as described for diffuse pericarditis. A localized pericarditis on the anterolateral aspect of the ventricles produces positive RS-T junction displacements in precordial leads at positions 4, 5, and 6, and discordant displacements in the extremity leads, upward in Lead I and downward in Leads II and III. As will be shown presently, these are precisely the kind of injury effects observed in recent anterolateral infarction.

The dictates of eqn(6-4) may be used to formulate a rule which is useful in anticipating the injury effects of the extremity leads. i.e., the spatial axis of injury $s\hat{E}_i$ points during systole in the direction of a line drawn from the center of the involved ventricle toward the center or centroid of the injured region, whereas the magnitude of $s\hat{E}_i$ is pro-

portional in length to the area circumscribed by the boundary of the injured lamina.[21] Moreover, the projection of $s\hat{E}_i$ upon the triaxial reference plane gives the manifest axis of injury $\hat{E}_i$, which defines by its projections upon the reference axes the direction and proportional magnitude of the RS-T junction displacements of the extremity leads. Thus, in the case of acute diffuse pericarditis, the configuration of the injured lamina is such that the centroid lies between the center of the ventricles and the cardiac apex. In connection with further use of the rule, it is important to note that a localized pericarditis, confined to the strictly anterior aspect of the ventricles or to the strictly posterior aspect of the ventricles, produces an axis of injury $s\hat{E}_i$ which is directed normal to the plane of the triaxial reference system. Consequently, $\hat{E}_i$ is zero and no RS-T junction displacements appear in the extremity leads. It also follows that two areas of acute local pericarditis, confined to diametrically opposite aspects of the ventricular walls, are associated with two axes of injury, like in magnitude and unlike in sign (or of inverse direction). Their resultant is zero, and no associated RS-T junction displacements appear in the extremity leads.

Let us conclude the present argument with the example of stab wound of the ventricles. The injured lamina conforms in its configuration to that of the surface of the penetrating instrument (provided no important subdivision of the coronary arteries is severed). If penetration of the wall is subtotal, the boundary of the injured lamina conforms to the hole in the epicardial surface. Obviously, because of the size of the instruments ordinarily used, S_i is small, and, consequently, $s\hat{E}_i$ is small, so that the anticipated RS-T junction displacements of the extremity leads are likely to be negligible. If penetration of the wall is total, the injured lamina has a tubular configuration, with a boundary at the epicardial, and a boundary at the endocardial, surface. Moreover, the boundaries are approximately similar geometrically. When each boundary is treated separately, as if the other opening of the injured lamina were closed, two forces are derivable which are like in magnitude and unlike in sign (of inverse directions). Their resultant is zero, and, consequently, total, as compared with subtotal, penetration is less likely to produce RS-T junction displacements in the extremity leads. When striking displacements are found before operation, it is best assumed that an important subdivision of the coronary arteries is severed. The subepicardial muscle is very susceptible to trauma, and may act as if it were injured when the epicardial surface is handled gently or even wiped with moist gauze. Under the circumstances, the circumferences of the injured laminae are large, and the electrical effects that are produced may be striking. However, the trivial nature of such injuries results in effects of brief duration, and striking RS-T junction displacements may vanish in a few hours or even in a few minutes. These factors are considered essential for proper interpretation of electrocardiograms from subjects with stab wound of the heart.

ON THE ELECTROCARDIOGRAPHIC EVOLUTION OF MYOCARDIAL INFARCTION

The QRS changes associated with myocardial infarction have been ascribed to the absence during systole of the electrical forces which were previously present in the dead zone. It is necessary to modify this statement at the present time. Fundamentally, two kinds of QRS changes are ordinarily associated with myocardial infarction, i.e., transient and permanent. The latter are ascribed to the absence of forces that were previously present in the dead zone. Throughout the injured zone, regression consists of a subnormal change of polarization.[21] Consequently, the electrical moments of that subdivision of the accession wave which passes through the injured zone are of reduced magnitude as long as the injured zone persists. Ultimately, part of the injured zone may die and thus increase the dimensions of the dead zone and the magnitude of the permanent QRS changes. In many instances it is highly probable that most of the injured zone vanishes by passing into the ischemic state. Transient QRS changes associated with infarction are ascribed to the diminished magnitude of forces which had been previously great during accession of the injured zone. The subsequent disappearance of the injured zone is attended by the return to normal magnitude of accession forces that were previously small throughout the injured zone. Concurrently, there occurs a subtotal return of QRS changes toward a more normal form.

In the initial stages of impaired coronary flow, the region of diminished irrigation may pass at once into first grade ischemia. The electrocardiogram at this time reveals only striking primary T-wave changes (Fig. 8, *a*). At a variable period of time thereafter, the more central regions of the zone of first grade ischemia pass into second grade ischemia or into the injured state. Provided the injured zone extends to the epicardial surface, RS-T junction displacements of injury appear in the completed record. Potentially transient QRS changes concurrently develop. Inasmuch as the development of the injured zone is dependent upon subtotal conversion of the ischemic zone, the early primary T-wave changes subtotally disappear (Fig. 8, *b*). If the patient is fortunate, normal coronary flow may be re-established, whereupon the injured zone returns to the ischemic state and the latter subsequently vanishes (Fig. 8, *a*). Throughout such a period, the clinical phenomena which are associated with death of heart muscle (fever, leucocytosis, increased sedimentation rate, and fall of blood pressure) are absent. In more unfortunate subjects infarction develops, whereupon extension of the injured zone continues until only a small semiperifocal zone of ischemia remains. Thus, striking RS-T junction displacements appear, together with more definite QRS changes, and the initial primary T-wave changes may now be absent except in unipolar or semiunipolar leads recorded with the exploring electrode super-

jacent to the zone of local ischemia. In similar leads recorded with the exploring electrode superjacent to the injured zone, the RS-T junction displacements are maximal and positive.

The reasons for a relatively limited extension of the injured zone in the direction of the neighboring endocardial surface are the same as those which determine a like distribution of local ischemia, and are set forth in Section V. At such a time, when the injured state involves a maximal area of subepicardial muscle and the neighboring subendocardial muscle is as yet uninvolved, the magnitude of the RS-T junction displacements is maximal. At some critical stage of extension of the injured zone, death of its more central regions occurs. At this time the clinical picture of acute infarction is complete. The severity of the clinical manifestations depends upon the rate of development of the various stages and to a less extent upon the volume of muscle involved. The dead zone may remain stationary or extend beyond its initial size. In event of the latter, the associated QRS changes progress.

During the early stages of healing (ordinarily two to four weeks after infarction in man), the injured zone diminishes in the direction of the dead zone because of the passage of its peripheral units from the injured, back into the ischemic, state. Consequently, when the injured zone is no longer in contact with the epicardial surface, the RS-T junction displacements will have vanished, together with most of the temporary QRS changes. Inasmuch as the subepicardial units of the ischemic zone have been increased by conversion of injured units into the ischemic state, the associated primary T-wave changes subtotally reappear. Finally, during the months which follow, the ischemic zone diminishes in the direction of the dead zone because of the gradual return of its units to the normal state. Concurrently, the final primary T-wave changes vanish, and only the permanent QRS changes, associated with the dead region, remain. Certain of the foregoing statements need clarification, but before entering the more profound aspects of the problem it is suggested that the reader refer to Fig. 9 for a diagrammatic summary of the critical stages of infarction.

At the present time it is not generally recognized that, from a fundamental standpoint, stages *A* through *B* of Fig. 9, *a* constitute the

Fig. 8.—(*a*) Primary T-wave changes of local ventricular ischemia: Curves A and B were recorded, ten days apart, from a 40-year-old subject who was hospitalized at the time because of severe heart pain. There are no definite changes which can be ascribed to muscle in the injured or in the infarcted state. The local ischemia is more intense at the time of the B recording, where the manifest gradient has undergone a striking negative rotation. The ischemia is anterolateral or in the muscle ordinarily irrigated by the left coronary artery. The subject had no fever, leucocytosis, fall of blood pressure, or increased sedimentation rate. Curve C was recorded after an asymptomatic interval of two months, and is regarded as normal. (*b*) Primary T-wave changes and RS-T junction displacements, with minor QRS changes, in a subject who had no clinical evidence of myocardial infarction: The subject, 42 years of age, had suffered severe heart pain throughout the twelve-day period over which curves A, B, and C extend. Curve D was taken one week after C, at a time when pain was absent. Curve A is typical of anterolateral ischemia. In curve B, at the time of maximal pain, a definite injury effect is present in Lead IVF. Here the primary T-wave changes have subtotally disappeared. Throughout curves C and D the injury effects vanish, and the T-wave changes again become pronounced. It is held that the subject narrowly missed having myocardial infarction at the time of the B recording.

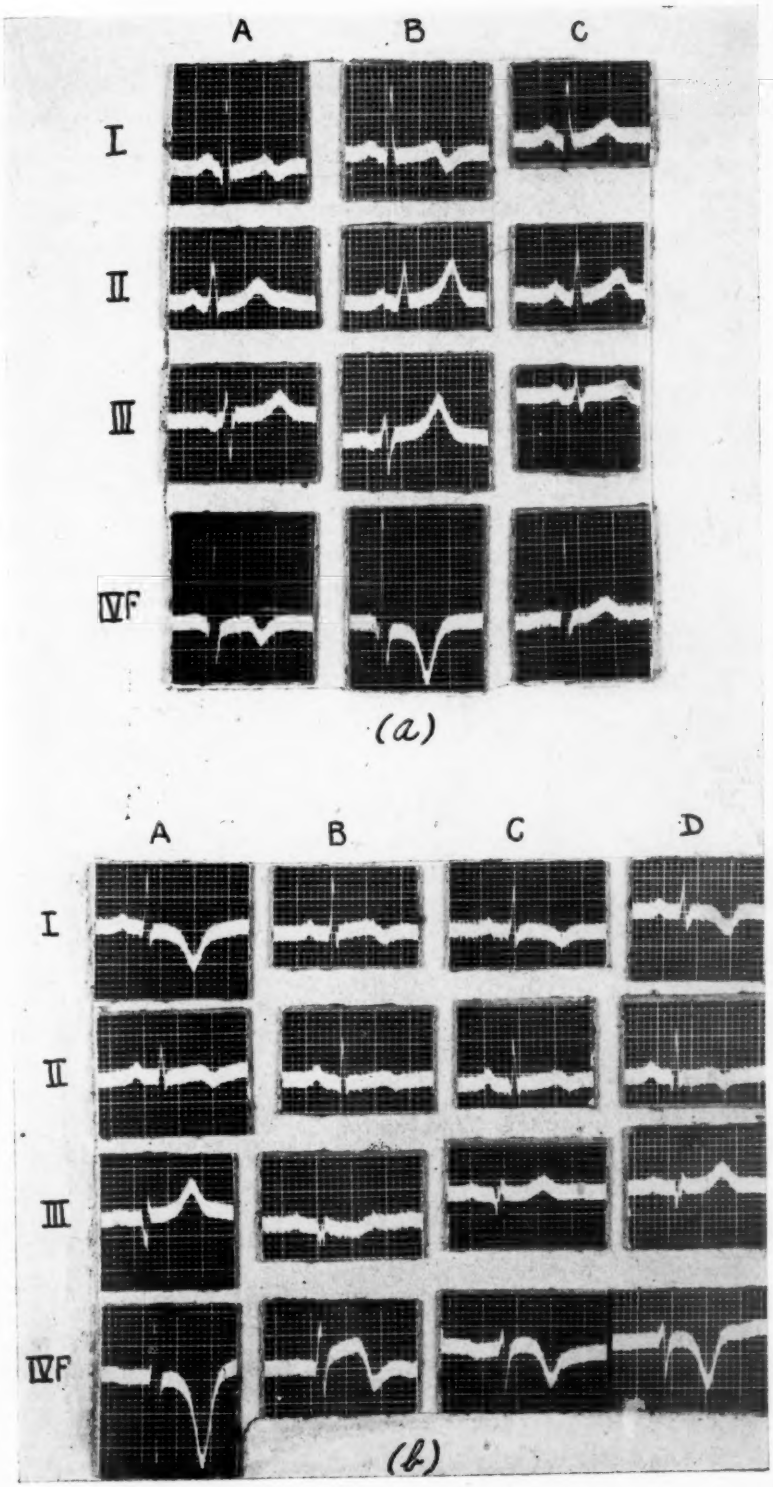


Fig. 8.—*(For legend see opposite page.)*

physiologic basis of the early myocardial changes associated with infarction. The electrocardiographic changes which accompany stages *A* and *B* consist of primary T-wave changes caused by acute local ventricular ischemia, and, as previously pointed out (Section V), are the result of a diversion of the gradient. In stage *B*, a zone of injury has appeared without affecting the completed record. Fig. 9, *c* illustrates the manner in which the zone of acute (or chronic) local ventricular ischemia may be treated for purposes of analysis. The zone of local ischemia is limited at first by the interface which separates it from normal muscle. After further expansion it becomes limited, in addition, by the epicardial surface. If and when the ischemic zone extends to the endocardial surface, it is necessary that the circumference of its epicardial surface boundary exceed the circumference of its endocardial surface boundary in order that the average duration of the excited state within the former boundary shall exceed that within the latter boundary. The zone of ischemia is divided into lamellae of elementary thickness. Throughout any single lamina the duration of the excited state is uniform. If lines are drawn, commencing upon the periphery of the ischemic zone, inward toward the point or points of maximal ischemia, and are made to cut all encountered lamellar surfaces at right angles, the direction of the lines describes the direction of the most rapid space rate of increase of effective duration of the excited state. Neglecting the influence on regression produced by the local order of accession, the direction of the lines determines the direction of local regression. The negative regression potential at a point p, nearby, and outside the heart, may be regarded as proportional to the sum of the negative solid angles subtended at p by the epicardial surface boundaries of the open ischemic lamellae. If some of the lamellae are likewise open at the endocardial surface, the potential at p will be less negative by a value proportional to the sum of the positive solid angles subtended at p by the specified endocardial surface boundaries. Inasmuch as the solid angles which measure the regression potential are independent of the configuration of the surfaces of the lamellae whose boundaries subtend them, the regression potential at p depends only upon the second reversal of polarization of the surface muscle units. Regression of the lamellae which are closed or which lie between the surfaces makes no contribution to the regression potential outside the ventricular wall. In short, the regression potential at an instant is proportional to the difference of potential due to the change of polarization at the epicardial surface as compared with that at the endocardial surface. That a change of polarization is likewise present between these surfaces is immaterial.

In stage *A* (Fig. 9, *a*), when the zone of ischemia does not touch the epicardial or endocardial surface, all of the lamellae are closed. A zone of ischemia of this kind cannot alter the order of regression of the muscle units at the ventricular surfaces, an order which alone determines the form of T.[22]

In Fig. 9, *d* the injured zone is treated in a fashion similar to that described for the ischemic zone. The lamellae into which the injured zone is subdivided represent regions throughout any one of which the subnormal change of polarization during regression is everywhere the same. If the subnormal change of polarization is regarded as having occurred initially during accession, rather than regression, the effect on the completed record is essentially the same, although the process is one of gradual blocking, and although no injury current flows. As pointed out elsewhere,[21] it appears unlikely that a blocking process is the rule. The lines (Fig. 9, *d*) which commence upon the dead zone and radiate toward the periphery of the injured zone, and which cut all encountered lamellar surfaces at right angles are the paths along which there

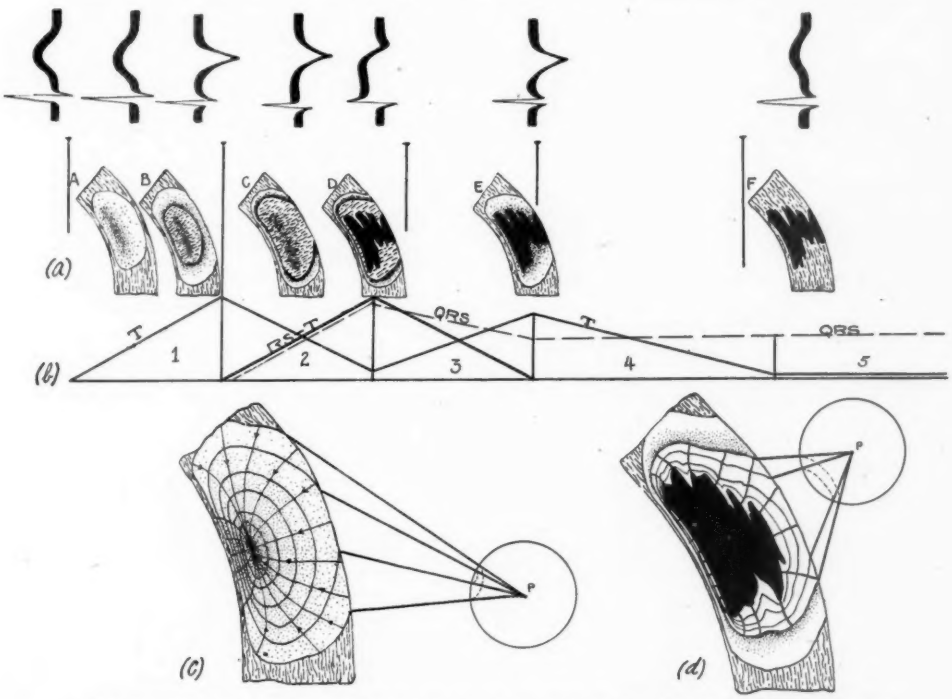


Fig. 9.—(*a*) Blocks of muscle A, B, C, D, E, and F depict the evolution ascribed to myocardial infarction. Superimposed are curves which display the associated electrocardiographic changes as produced in a unipolar lead from a superjacent point. In block A, local ischemia has developed without producing detectable electrical effects. In block B, ischemia has reached the epicardial surface and has accounted for a primary T-wave change. An injured zone has also appeared within the ischemic zone, and theoretically minor QRS changes may be present. In block C, the injured zone has reached the epicardial surface, so that RS-T junction displacements, further QRS changes, and reduced T-wave changes are present. In block D, infarction has occurred, and RS-T junction displacements are maximum. Concurrently, the primary T-wave changes are reduced to a minimum. In block E, healing has commenced. The injury zone has vanished and the effects of local ischemia are again pronounced (compare curves three and six from the left). In block F, the infarct is depicted as healed. No perifocal ischemia is present. (*b*) Diagram showing the time relationship of the appearance and (or) disappearance of the various kinds of electrocardiographic changes, QRS, T, and RS-T junction, which characterize the electrocardiographic evolution of myocardial infarction. Note the reciprocal relationship between primary T-wave changes and RS-T junction displacements, which is likewise shown by the development, at the epicardial surface, of the two zones, ischemic and injured. See text. (*c*) Showing the lamellar character of the ischemic zone and its relationship to the regression potential produced at a superjacent point p. (*d*) Showing the lamellar character of the injured zone and its relationship to the injury potential produced at a superjacent point p. See text.

exists the greatest space rate of change of subnormal polarization during the resting, and again during the excited, state. It is clear that, until the injured zone extends to the epicardial surface, all of its lamellae are closed. Consequently, during the resting, and again during the excited, state, no field of injury exists outside of the ventricular wall. It is likewise clear that, when the injured zone is transmural, the injury potential outside the ventricular wall is a function of the difference between the subnormal change of polarization at the epicardial surface and that at the endocardial surface. The subnormal change of polarization in units between these surface layers is immaterial.[21]

The spatial axis of injury $s\hat{E}_i$ is proportional in length to the areas circumscribed by the boundaries of the open laminae of the injured zone, and is directed (during systole) from the center of the involved ventricle toward the center or centroid of the injured zone.

In stage *C* of Fig. 9, *a*, the area circumscribed by the epicardial boundary of the injured zone has expanded at the expense of the area circumscribed by the epicardial boundary of the ischemic zone. Consequently, the appearance of RS-T junction displacements (dependent upon the former area) are accompanied by a subtotal disappearance of primary T-wave changes (dependent upon the latter area). Obviously, as the accession wave traverses the subnormally polarized injured zone, the magnitude of the local accession forces is proportionally subnormal, and, consequently, QRS changes concurrently appear.

The initial development of local ischemia and injury may be regarded as proceeding to the stage (*C* of Fig. 9, *a*) at which a dead region is about to appear, and, being reversible, may be looked upon as producing the transient variety of electrocardiographic changes that are observed in certain patients with angina pectoris. However, if the process is regarded as introducing myocardial infarction, the zones specified are responsible for changes which are best described as evidence of impending infarction. The evolution through which the changes may proceed or the time they may last and yet be unattended by the appearance of a dead region (actual infarction) is not known. Clinicopathologic observations make it certain, however, that an evolution which stops short of the injury effects may exist for several weeks, and possibly several months, and be unattended by the development of a dead zone.[19] If the evolution proceeds rapidly, and promptly reverses, the stage of RS-T junction displacement may be reached without the occurrence clinically of evidence which is considered characteristic of actual infarction.

Including the electrocardiographic changes herein described as evidence of impending infarction, the electrocardiographic evolution of myocardial infarction may be described in five fundamental stages: (1) the initial diversion of the gradient $\hat{G}$, which is a measure of the appearance of the primary T-wave changes; (2) the development of the axis of injury $\hat{E}_i$, a concurrent subtotal reversion of $\hat{G}$, and a concurrent

diversion of $\hat{A}_{QRS}$, which measure, respectively, the appearance of RS-T junction displacements, the subtotal disappearance of the primary T-wave changes, and the appearance of QRS changes; (3) the decay of $\hat{E}_1$, the concurrent second diversion of $\hat{G}$, and the concurrent subtotal reversion of $\hat{A}_{QRS}$, which measure, respectively, the disappearance of RS-T junction displacements, the reappearance of primary T-wave changes, and the subtotal disappearance of QRS changes; (4) the final reversion of $\hat{G}$, which measures the final disappearance of the primary T-wave changes; and, finally, (5) the permanent persistence of a diversion of $\hat{A}_{QRS}$ and $\hat{A}_T$, which measure the permanent QRS changes and the permanent secondary T-wave changes.

Ordinarily, stage 1 is traversed rapidly in the case of infarction, so that the initial electrocardiograms display changes characteristic of stage 2 or stage 3. Stage 4 continues for a relatively long period of time, and the associated changes are usually referred to as evidence of healing of the infarction. In a single curve, the changes associated with stages 2 and 3 may closely resemble one another, and other clinical criteria must be used to ascertain the presence or absence of myocardial infarction. When stage 5 has been reached, infarction is said to be healed.

SUMMARY AND CONCLUSIONS

As pointed out more than a decade ago by F. N. Wilson and his coworkers, the well-established laws which define the flow of electric currents in homogeneous volume conductors are applicable to the interpretation of the electrical effects produced by the heartbeat with sufficient accuracy to be of (great) clinical usefulness. An analytical approach to the problem is herein made by a method of geometric visualization which should prove useful to those who are not familiar with advanced mathematics. A few footnotes are included; they contain some of the more profound aspects of the problem and support much of the material, but they may be neglected by those who are interested only in a clinical use of the analysis.

The properties of vectors are defined, and the three required manipulations are discussed. The characteristics of the electrical field are briefly considered in relation to a point source and in connection with the excitable cell. The instantaneous electrical axis is defined and its use illustrated.

Ventricular accession is considered inductively, and the critical formations of the QRS sÊ-loop of the vectorcardiogram are derived synthetically. Important relationships between the loop and the extremity leads are pointed out. The effects on the loop and those on the extremity leads produced by hypertrophy, block, and muscle death are analyzed. The unipolar and semiunipolar leads are considered analytically.

The manifest and spatial mean axes are defined and discussed, with particular emphasis on their value in the interpretation of the primary

and secondary T-wave changes. Certain clinical and analytical manifestations of local ventricular ischemia are considered. It is pointed out that the primary T-wave changes which frequently attend acute nephritis in transient form and those which attend chronic hypertension in more permanent form are strikingly similar to those which indicate local ischemia of muscle that is ordinarily irrigated by the left coronary artery.

The electrical effects produced by an injured lamina are discussed in relationship to pericarditis and stab wounds of the heart. Finally, the electrocardiographic evolution of myocardial infarction is considered, and the similarity of certain early stages to certain late stages is stressed.

In order to accomplish the task, it became necessary to introduce much which is not new, but which is scattered within various sources that have appeared at intervals over a considerable period of time. The method of analysis, as set forth, has proved useful to the author over a period of years both for diagnostic and teaching purposes. Moreover, the uniformly accurate diagnostic results obtained, particularly in problems of local myocardial ischemia and infarction, appear to completely justify the adoption by Wilson, et al., of certain well-established physical laws for interpretation of the electrical effects produced by the heartbeat.

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Clinical Reports

COARCTATION OF THE THORACIC AORTA WITH AN ANEURYSM DISTAL TO THE OBSTRUCTION

Report of a Case

Jerry Zaslow, M.D., and Sidney O. Krasnoff, M.D.
Philadelphia, Pa.

IN A review of the literature up to September, 1942, only two cases of aneurysm of the aorta distal to a coarctation were found.[1, 2] This paper presents a similar case in a 25-year-old white man.

CASE REPORT

D. Y., a 25-year-old white man, was apparently in good health until one year prior to admission to the Jewish Hospital in Philadelphia. At that time an increase in the size of the base of the heart was found during a routine physical examination. A roentgenogram revealed a prominence in the region of the aortic knob. Several serologic tests for syphilis were negative. One week before admission to the hospital the patient developed an upper respiratory infection, followed by a persistent cough. About 7 A.M. on the day prior to admission, the patient awoke with a feeling of malaise and pain in the left shoulder. During the day the pain became worse, stabbing in nature, and radiated over the precordium to the left upper quadrant and left loin. He was nauseated, but did not vomit. At 4 A.M. on the day of admission, the patient had a severe precordial pain and collapsed. He was admitted to the hospital at 5:20 A.M. on Feb. 20, 1943. There were no further contributory facts in the history.

Physical examination on admission revealed a well-developed and well-nourished white man in severe pain. He was oriented and cooperative. The oral temperature was 102° F. The radial pulse rate was 90 per minute. The respiratory rate was 28 per minute. The blood pressure was 110/80 in the right arm and 108/76 in the left arm. Examination of the head, eyes, ears, nose, and throat revealed no abnormalities. There were a few râles at the base of the right lung posteriorly. The apex beat of the heart was 10 cm. to the left of the midsternal line in the sixth intercostal space. The base of the heart was enlarged to percussion, measuring 10 cm. transversely. The heart sounds were regular, rapid, and well heard. There were no murmurs, shocks, or thrills. The abdomen and extremities appeared normal. Because of the poor

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condition of the patient, the neurologic examination was limited. However, the deep reflexes were normal, and no abnormal reflexes were elicited.

The patient was given $\frac{1}{6}$ grain of morphine sulfate and $\frac{1}{200}$ grain of atropine sulfate hypodermically. In a few minutes the patient became dyspneic, and started to cough and expectorate greenish-black mucus. At 8:15 A.M., he became restless, thrashed about, gasped violently for air, became very pale, and was soon pulseless. In spite of stimulants, the patient died at 8:30 on the morning of admission.

Post-mortem examination was performed by one of us (J. Z.) two hours after death.

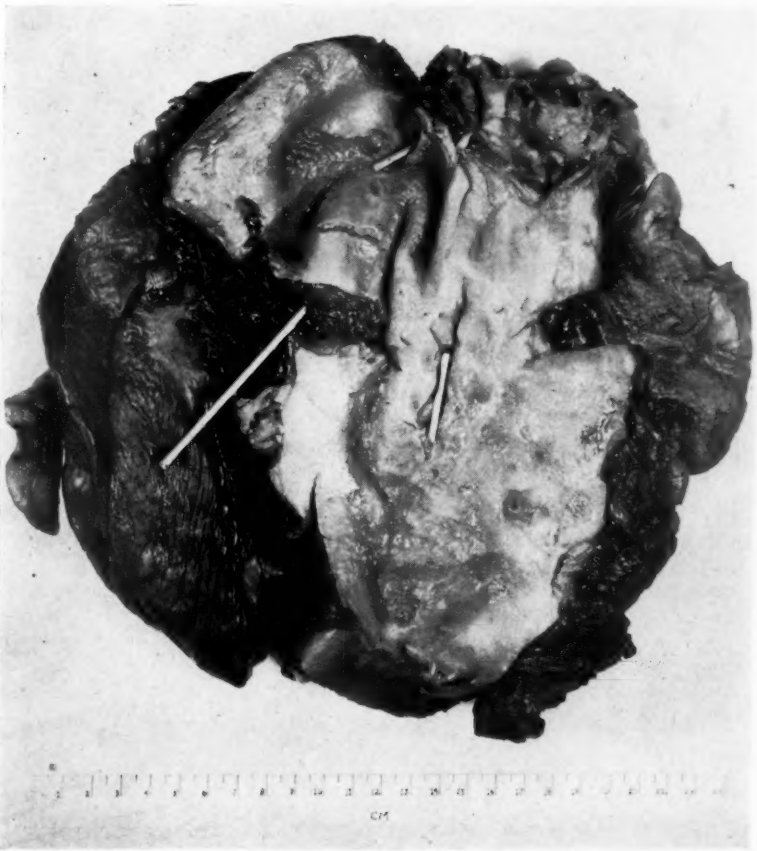

Fig. 1.—View of the descending thoracic aorta. The lungs lie at both sides of the opened vessel. The uppermost indicator is coming out of the coarcted area. Note the appearance of an obstructing band at this point. The left lower indicator points to the area of fatal, terminal rupture. The right lower indicator lies in a deep tear in the intima. Note the presence of numerous other rents in the intima. However, none of these invade the media. There was no evidence of any inflammatory process in any portion of the vessel.

POST-MORTEM OBSERVATIONS

The body was that of a well-developed white man, 25 years of age. External examination revealed only extreme pallor of the mucous membranes.

The left pleural cavity contained about 4,000 c.c. of blood and blood clot. The right pleural cavity was normal. The posterior mediastinum and the upper portion of the retroperitoneal area of the abdominal cavity contained clotted blood. The pericardial cavity contained no blood or serous fluid.

The heart weighed 410 grams. The muscular tone was good. The left ventricular wall measured 15 to 19 mm. in thickness. The right ventricular wall averaged 3 mm. in thickness. The ventricular cavities appeared normal. The auricular appendages contained no thrombi. All of the valves and coronary vessels were normal. The aortic valve showed no spreading of the commissural angles and no thickening of its free margins. The ascending aorta and transverse portion of the arch were normal in diameter and appearance . At the junction of the transverse with the descending thoracic aorta, there was a constriction of the lumen, as if by a fibrous band. The diameter of the lumen at this portion was 7 mm. From this point caudad, the lumen was markedly increased in size, measuring 20 cm. in circumference at its widest portion. The dilatation had a fusiform appearance. It extended for a distance of 15 cm., almost reaching the diaphragm. Opening the vessel disclosed a transverse rent in the wall 3 cm. in length at the midportion. This was the source of the bleeding. There were numerous other tears of the intima, but these were not deep (Fig. 1). The abdominal aorta was normal. The branches of the thoracic aorta proximal to the obstruction were slightly dilated, but no erosion of the under surfaces of the ribs was seen.

The left lung showed only compression atelectasis. The right lung was congested. All the other organs appeared normal, except for marked pallor.

Microscopic examination of the coarctation showed an excessive amount of fibrous tissue beneath the intima. There was no evidence of any active inflammatory process. Sections from the aneurysm revealed no signs of syphilis or atherosclerosis. The media showed patchy areas of mucinous degeneration. The intima appeared normal. There was some thickening of the subintima.

COMMENT

The coarctation was at the point where the ductus arteriosus meets the aorta. During obliteration of the ductus there must have been an extension of the fibrotic process into the aorta. This appears to have been the case because microscopic examination of the stenotic area showed only fibrous tissue beneath the intima. In the case reported by Hecker,[2] the coarctation was in the same location. The sequence of events in the formation of the aneurysm is more difficult to understand. It may be that the eddy formation just distal to the constriction resulted in a weakening of the aortic wall and a gradual dilatation of the lumen. This was progressive over a period of years. Eventually, because of some excessive strain (coughing), there was a sudden increase in the pressure within the sac, with rupture of the weakened wall. The presence of numerous tears in the intima, in addition to the ruptured area, suggests that there must have been a rather sudden increase in pressure within the aneurysm.

SUMMARY

1. Aneurysm of the aorta distal to a coarctation is uncommon.
2. A case which occurred in a 25-year-old white man is presented.
3. A possible explanation for the anatomic abnormalities is offered.

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CHRONIC OCCLUSIVE ARTERIAL DISEASE (ARTERIOSCLEROSIS OBLITERANS), ASSOCIATED WITH RETINITIS PIGMENTOSA

Case Report

Jack L. Eisaman, M.D.
Bluffton, Ind.

RETINITIS PIGMENTOSA is apparently a vascular disease of the retina which is rarely associated with generalized peripheral vascular disease. A search of the literature concerning peripheral vascular disease associated with retinitis pigmentosa revealed only one article.[1] The scarcity of this pathologic combination makes the following case of interest.

Since the discovery of the ophthalmoscope the cause of retinitis pigmentosa has been disputed . Among the numerous theories of its causation that have been advanced are toxic or endocrine factors, trauma from light, and avitaminosis. It is not the purpose of this report to discuss the etiology, but to point out that whatever the process, whether it be one of localized susceptibility, choroidal sclerosis, or endogenous influences, the vascular changes may be of a general and peripheral nature, rather than just localized in the retinas.

CASE REPORT

J. R. P., a railroad brakeman, aged 56 years, married and the father of two healthy children, was first seen in July, 1942. His mother died at 45 years of age from puerperal sepsis; his father died at 91 years of age. He had six siblings, one of whom was known to show no evidence of retinitis pigmentosa. The patient could give no family history of this condition. His past history was negative except for influenza in 1917 and an accident which had occurred two years before. He knocked a fragment from his left knee cap and fractured his left elbow and some ribs. His leg was in a cast for three weeks, and it was after this cast was removed that he first noticed the left leg becoming smaller. For years he had smoked one or two packages of cigarettes daily and used alcohol occasionally.

His chief complaints were of pain in his left leg and exhaustion. These first appeared during the latter part of the previous winter. He noticed coldness of his left foot. If he would put his foot on a locomotive fire box, he could keep it warm. Both legs cramped after exercise, but the left one was always worse. It seemed strange to him when warmer weather came that his foot continued to be so cold and his leg tired so easily. A week previous to admission he had been mowing the lawn for an hour, when he developed a sharp pain in his left leg and a cramp in its calf. Rest and massage gave relief. When he tried to

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push the mower again, he was able to go only 50 feet before the pain and cramp returned. After ten minutes he was at ease. At rest he suffered no pain. Walking only half a square precipitated the pain. He had lost 13 pounds in the preceding year and noticed considerable exhaustion for six months. Otherwise, his history was essentially negative.

Physical examination revealed a 56-year-old man, 129 pounds in weight and 67 inches in height. His mouth was edentulous, with only an upper plate. The eye grounds were described by the ophthalmologist* as typical of retinitis pigmentosa. The patient's heart sounds were distant. The blood pressure was 125/80. The ulnar pulsations were diminished on both sides. Neither the dorsalis pedis nor the posterior tibial pulse was palpable on the left. The left foot was much paler than the right, and the left lower extremity appeared definitely smaller than the right. The femoral pulsations were equal and of good quality.

TABLE I

LEG MEASUREMENTS ON JULY 13, 1942.

SITE	LEFT (INCHES)	RIGHT (INCHES)
6 inches above patella	14¾	16¾
6 inches below patella	12¼	12⅞
Lower extremity	36½	37

Table I shows that the left lower extremity was definitely smaller than the right, especially above the knee.

TABLE II

OSCILLOMETRIC INDICES ON JULY 13, 1943

SITE	LEFT	RIGHT
Popliteal	1	2½
Anterior tibial	0	3

The oscillometric indices listed in Table II show absence of the deep circulation in the area supplied by the anterior tibial artery of the left leg.

TABLE III

SKIN TEMPERATURES, MEASURED WITH A GENERAL ELECTRIC THERMOCOUPLE ON JULY 13, 1942

SITE	LEFT (DEGREES)	RIGHT (DEGREES)
Ball of foot	84½	84½
Dorsum of foot	89½	91½
Mid-calf	89½	91½
Mid-thigh	94½	95

The skin temperatures listed in Table III reveal that the left lower extremity was not completely adjusted to a deficiency of the deep circulation.

The hemoglobin was 15 Gm., the erythrocyte count, 5.36 million, and the leucocyte count, 9,200, with a fairly normal differential count. The

*H. Brooks Smith, M.D.

Mazzini flocculation test was negative, the blood urea nitrogen, 16.3 mg. per cent, and blood sugar, 80 mg. per cent. Urinalysis was negative, and the basal metabolic rate was +9 per cent. The prostatic secretion contained a few pus cells, and culture revealed gram-positive cocci in pairs and tetrads.

Dental roentgenograms revealed no disease. The electrocardiogram and chest roentgenogram showed nothing abnormal. Roentgenograms of the lower extremity from above the knee to, and including, the foot showed no definite areas of calcification. There was one small area of calcification just below the head of the fibula and between the tibia and fibula which might have been in the anterior tibial artery.

SUMMARY

A case of retinitis pigmentosa, associated with chronic, occlusive, peripheral vascular disease, is presented. Although the cause of retinitis pigmentosa is still disputed, this case suggests that the pathologic changes in the retinae may not be localized there, but may occur as a part of a similar disorder elsewhere in the body.

REFERENCE

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Abstracts and Reviews

Selected Abstracts

Keys, A., Stapp, J. P., and Violante, A.: Responses in Size, Output and Efficiency of the Human Heart to Acute Alteration in the Composition of Inspired Air. Am. J. Physiol. **138**: 763, 1943.

The results are reported from numerous experiments in which acute hypoxia was produced in twenty-seven normal young men. All studies were made under constant environmental conditions with the exception of the partial pressures of the gases in the inspired air. In most cases the pO_2 corresponded to that at 18,000 to 28,000 feet altitude; in some cases CO_2 at 14 to 30 mm. Hg was present. Some experiments were made with inspiration of pure oxygen. Exposure lasted from 10 to 48 minutes.

From roentgenkymographic measurements it is concluded that cardiac dilatation does not take place under these conditions. The stroke volume remains nearly constant in this acute hypoxia and the minute output of the heart is increased only slightly more than in proportion to the pulse rate change. Cardiac efficiency is unimpaired.

Carbon dioxide increases the altitude tolerance, and in hypoxia with CO_2 added the pulse rate increases less than without it. Again, the heart does not dilate and the stroke volume tends to remain constant.

Respiration of oxygen at four to five times the normal pO_2 results in a slight decrease in cardiac "work" and "effort" with no significant change in heart size or efficiency.

Blood pressure responses have no certain predictive value as to whether syncope is to occur. In the present series complete syncope occurred in ten cases. There is always a relative bradycardia in recovery from hypoxic syncope.

Indications were seen that acute hypoxia disturbs the stability of the autonomic nervous system.

It is concluded that, in normal young men, attempts to strengthen or safeguard the heart under hypoxic conditions would serve no useful purpose. The heart does not seem to be the limiting factor in tolerance to acute hypoxia.

AUTHORS.

Marcuse, F. L., and Moore, A. U.: Low Heart Rate in the Newborn Rat. Am. J. Physiol. **139**: 49, 1943.

One-day-old rats, when compared with 120-day-old (tamed) rats, were found to have a significantly lower heart rate and less fluctuation in heart rate. Sex differences present in the tamed, mature animals were not present in the 1-day-old animals.

In the first 24 hours of life significant changes in heart rate were observed. In a twenty-one-day period of daily heart recordings, it was observed that heart rate increased steadily in the first 11 days of life; a plateau of no increase in rate prevails from the eleventh to twenty-first days; sex differences manifest themselves with increasing clarity from the tenth day on.

AUTHORS.

Wiggers, H. C., Glaser, G. H., Canavarro, K. de S., and Treat, A. E.: Arterial and Central Venous Pressure Changes Following Complete Transection of the Spinal Cord (C_8-T_1). Am. J. Physiol. 139: 217, 1943.

This study concerns the acute arterial hypotension and associated phenomena which occur following transection of the spinal cord (C8) of supine lightly anesthetized cats. When the transection procedures were uncomplicated by severe hemorrhage, pressures did not descend to critical levels. The hypotension developed after the skeletal musculature of the thorax, abdomen, and hind limbs, which supposedly support the elastic postarterial vessels, had been rendered completely flaccid. Apparently, however, the venous return of these supine animals was not impaired by the loss of this extravascular support. The criteria for this concept are based upon the fact that atrial and effective venous pressures were, if anything, slightly elevated, while the heart rates remained tachycardic. The slopes of the ascending limbs of arterial pressure pulses revealed no changes indicative of an impaired stroke output.

In explaining the equivalent decrease of systolic and diastolic pressures on a hemodynamic basis, it was deduced that reduction of peripheral resistance is a major contributing factor, but that some additional dynamic event must be involved. The analysis suggests that an increase in the capacity of the aorta and its immediate large branches is involved. The acute hypotension following spinal transection may be considered to result from an increase in the capacity of and a reduction in resistance to blood flow throughout the entire arterial system from the root of the aorta to the capillaries. There is no evidence to support the postulate that an impairment of skeletal muscle tone or the extravascular mechanism is herein concerned with the fall in blood pressure in these supine animals.

AUTHORS.

Boyer, P. K., and Bailey, C. V.: Concentration of Carbon Dioxide in Expired Air in Heart Disease. Arch. Int. Med. 71: 529, 1943.

In man, regardless of age, sex, basal metabolism, or state of nutrition, the concentration of carbon dioxide in the expired air is strikingly constant.

Measurement of the concentration of carbon dioxide in the expired air during the determination of basal metabolism by the open circuit method is a valuable clinical aid in the study of the cardiac status and of the effectiveness of therapeutic measures; it is especially helpful in classifying patients with cardiac disease complicated by hyperthyroidism and obesity, in whom dyspnea on exertion is difficult to interpret; it is unique among methods of estimating cardiac function in that it is performed with the patient at rest; it measures the extent to which respiration compensates for circulatory failure.

AUTHORS.

Gubner, R., and Ungerleider, H. E.: Electrocardiographic Criteria of Left Ventricular Hypertrophy: Factors Determining the Evolution of the Electrocardiographic Patterns in Hypertrophy and Bundle Branch Block. Arch. Int. Med. 72: 196, 1943.

An electrocardiographic diagnosis of left ventricular hypertrophy can be made before advanced changes have occurred. Employing criteria established by a study of a large number of normal subjects and persons with hypertension, the authors found that the electrocardiogram is a valuable device for detecting left ventricular hypertrophy and is somewhat more sensitive than the teleoroentgenogram. The electrocardiographic and roentgen changes do not necessarily parallel

one another, and at times either may be relatively normal while the other shows definite evidence of hypertrophy.

Left ventricular hypertrophy may be considered to be present when left axis deviation occurs in association with any of the following changes:

1. Increase in amplitude of the QRS complex, best expressed by the sum of R_1 and S_3. Hypertrophy is present if this sum exceeds 2.5 millivolts and is probably present if it is over 2.2 millivolts. The increase in voltage is the earliest electrocardiographic change in hypertrophy.

2. Any perceptible depression of the S-T segment in Lead I, even of as slight a degree as 0.5 mm. (0.05 millivolt).

3. Lowering of T_1 below 1 mm., or further degrees of abnormality of T_1.

The changes in the S-T segment and the T wave may develop in the absence of left axis deviation, and left axis deviation is not an unvariable or necessarily integral part of the electrocardiographic pattern of left ventricular hypertrophy. It is shown that the usual occurrence of left axis deviation with left ventricular hypertrophy in hypertension is due largely to predominant obesity with transverse position of the heart, which in itself causes left axis deviation. In slender subjects with left ventricular hypertrophy, left axis deviation is not so often observed.

The increased amplitude of the QRS complex may most reasonably be attributed directly to an increased mass of left ventricular musculature. The changes in the S-T segment and the T wave are regarded as due to relative ischemia of the deeper layers of the left ventricle. This is occasioned by increased work of the heart without commensurate increase in coronary flow. Several factors, which are discussed, contribute to cause this disproportion.

The particular vulnerability of the subendocardial region of the left ventricle is due to an intramyocardial pressure gradient during contraction. During systole there is a marked increase in intramyocardial pressure in the deeper layers of the left ventricle, which exceeds aortic pressure and which obstructs coronary flow in this region, although there is no interference in coronary flow in the outer zone of the left ventricle or in the right ventricle or auricles, where the intramyocardial pressure does not rise above the arterial pressure. The subendocardial region of the septum and the left ventricle on this account is the area most vulnerable to ischemia. It is the site of predilection of myocardial disease when there is a relative insufficiency of coronary flow, as in hypertrophy, or when there is an absolute decrease in flow, as in coronary artery sclerosis and acute coronary artery occlusion.

Over a long period, the chronic subendocardial ischemia leads to irreversible changes, and replacement fibrosis occurs. This involves the Purkinje distribution network of the left bundle branch which ramifies in the subendocardial region of the interventricular septum and the left ventricle. Interference with left ventricular excitation caused by diffuse involvement of the conduction system leads to slurring, notching, and widening of the QRS complex, eventually progressing to the pattern of left bundle branch block, which is frequently encountered in association with long-standing and advanced left ventricular enlargement. The widening of the QRS complex is only in slight part attributable directly to increased thickness of the left ventricular myocardium.

Changes in the S-T segment and the T wave in Leads II and III, and, ultimately, right bundle branch block, occur in conditions associated with chronic right ventricular strain, such as pulmonic stenosis, cor pulmonale, and long-standing mitral disease. The pathogenesis of these changes, just as in left ventricular hypertrophy, is similarly related to ischemia of the subendocardial region of the right ventricle consequent to increased intraventricular pressure in the right ventricle.

AUTHORS.

Gardberg, M., and Ashman, R.: The QRS Complex of the Electrocardiogram. Arch. Int. Med. **72:** 210, 1943.

An analysis is presented of the QRS complex of the human electrocardiogram and of the variations in that complex which would appear when the heart is rotated to different positions within the thorax. Among different subjects there are considerable differences in the cardiac position within the thorax, and the effects of these differences are explained. In making the analysis, the authors have correlated experimental findings in the experimental animal, known effects of rotations of the heart in man produced by normal procedures or certain pathologic conditions, known effects of bundle branch block and of infarction in man, and information derived from studies of precordial leads. Less attention was given to the conflicting anatomic studies of the Purkinje system. In order to visualize the electrical events in three-dimensional space, clay models have been used.

The authors are convinced that, in a large majority of subjects, the directions of the electrical axes as revealed by the limb leads as projected on the frontal plane are correct within plus-minus 10 degrees, and the usual error may be less than this. It is pointed out that even if the error should be greater, the value of vector analysis is not thereby impaired in its more important applications.

AUTHORS.

Ungerleider, H. E., and Gubner, R.: Extrasystoles and the Mechanism of Palpitation. Tr. Am. Therap. Soc. **41:** 1942.

An analysis was made of 1,142 cases with extrasystoles in order to determine their clinical significance. In 58 per cent no objective evidence of heart disease was found.

Ventricular extrasystoles occur with considerable greater frequency than supraventricular premature contractions, and in the presence of heart disease there is still greater preponderance of ventricular premature contractions.

Several factors, which are discussed, increase the significance of premature beats. Among these are: the occurrence of premature beats of multifocal origin; frequent and persistent premature beats, particularly if they occur successively in short runs interrupting the regular rhythm; a definite increase in the number or shower of extrasystoles immediately following exercise; occurrence of premature contractions in the presence of a rapid heart rate; inversion of the T wave in the regular beat which follows the extrasystole; and postextrasystolic pulsus alternans.

Palpitation is a very common symptom often associated with extrasystoles. It has been generally attributed to an increased forcefulness of the regular beat following the premature systole, but several reasons are presented which indicate that this explanation is not tenable. It is suggested that palpitation occurring with premature contractions or tachycardia is due to, or associated with, an increased intensity of the first heart sound resulting from a more forcible closure of the atrioventricular valves. The symptom of palpitation is of no particular significance and occurs in normal subjects as well as in those with heart disease.

AUTHORS.

Solarz, S. D., and Eleck, S. R.: U-Wave Patterns in the Abnormal Electrocardiogram. J. Lab. & Clin. Med. **28:** 936, 1943.

In 1,000 cases with diagnostic electrocardiographic patterns, 94 cases of abnormal U waves were found. The U-wave patterns in these 94 cases showed the following chief characteristics:

a. In the left heart strain and in intraventricular block of the common type, the U-wave abnormalities consist of inverted U waves in Leads II and CF_4.

b. In the anterior wall infarction, abnormal (inverted or diphasic) U waves are found in Leads CF_2 and CF_4 with occasional similar abnormality in Lead I.

c. In posterior wall infarction, inverted U waves are found most commonly in Lead CF_4.

d. No abnormal U waves were found in right heart strain or in intraventricular block of the indeterminate S type.

A hitherto undescribed U-wave abnormality, a negative bowing of the T-P segment in Lead I, is discussed.

Instances of distortion of the T and P waves by large upright U waves and the confusion caused by the presence of prominent U waves in records of auricular fibrillation are pointed out.

Evidence is presented relating the presence of abnormal U waves to abnormalities of the S-T-T segment. In left heart strain and in the common type of intraventricular block, there is usually concordancy in the direction of the T wave, S-T deviation and U-wave direction. In posterior wall infarction there is concordancy of the deviation of the S-T segment and the direction of the U wave, but discordancy between T and U. In anterior wall infarction the reverse is true.

In serial records the abnormal U wave may undergo an evolution independent of the changes in the S-T-T segment.

AUTHORS.

Luisada, A. A.: On the Value of Mechanical and Acoustic Registration in the Diagnosis of Bundle Branch Block. Rev. argent. de cardiol. **9**: 169, 1942.

A clinical case is described in which mitral insufficiency caused by rheumatic endocarditis was associated with arteriosclerotic heart disease. The electrocardiogram indicated a right bundle branch block. On the contrary, acoustic and mechanical records, as well as fluoroscopy, gave evidence of a delayed left ventricular systole.

A diffuse bilateral lesion of the myocardium is admitted. The "right side" type of the electrocardiogram is explained by the right ventricular hypertrophy caused by the valvular lesion, in spite of the predominance of myocardial lesions on the left side.

Considerations on the value of jugular vein tracings in the differential diagnosis between "opening snap" of the mitral valve and third heart sound follow.

A splitting of the C wave of the jugular tracing confirms the existence of two different components of this wave, each related to the activity of one ventricle.

AUTHOR.

Moia, B., and Battle, F. F.: The Electrocardiogram Before and After Exercise Following the Ingestion of Food. Rev. argent. de cardiol. **9**: 339, 1943.

In thirty normal subjects, the electrocardiogram obtained within one hour after a common meal, before and after a standard exercise (climbing a sixty-step staircase), did not show any pathologic alterations.

In thirty patients suffering from typical or atypical attacks of angina pectoris, and with electrocardiograms which were normal or showed simple axis deviation but without signs of myocardial damage, the electrocardiograms, obtained at rest but within one hour after lunch, showed alterations characteristic of myocardial ischemia in 27.2 per cent of the cases.

After the ingestion of food, the performance of an exercise unable to provoke precordial discomfort (climbing at a moderate rate a 60-step staircase divided in three flights) gave positive results in 73.4 per cent of cases. The same exercise,

made several hours after lunch, produced definite electrocardiographic changes in only 23.3 per cent. In some of the patients in which this test was negative, the electrocardiographic changes appeared merely by eating.

The usefulness of obtaining electrocardiograms at rest or after a moderate exercise, within an hour of the ingestion of food, for the diagnosis of transitory myocardial ischemia, is emphasized.

The test is innocuous and produces no uncomfortableness.

The mechanisms by which the ingestion of food may originate or facilitate the appearance of the electrocardiographic changes described, are discussed.

AUTHORS.

Grier, G. W.: The Diagnosis of Congenital Heart Lesions in Children. Am. J. Roentgenol. **49:** 366, 1943.

As regards roentgen diagnosis, congenital anomalies may be divided into three classifications:

A. Those with characteristic roentgen appearance.

B. Those in which the appearance is either not characteristic, or else similar in different lesions.

C. Those in which the roentgen appearance is either normal or abnormal, but offers no help in differentiating the lesion.

AUTHOR.

Fisher, C. E., and Mulligan, R. M.: Quantitative Study of Correlation Between Basophilic Degeneration of Myocardium and Atrophy of Thyroid Gland. Arch. Path. **36:** 206, 1943.

A quantitative study has been made of basophilic degeneration of the myocardium in eight cases of atrophy of the thyroid gland, and in 142 control cases, of which 67 showed basophilic degeneration of the myocardium.

The number of muscle fibers affected by basophilic degeneration in an area of myocardium measuring 19.28 square millimeters was designated as the basophilic degeneration index (B. D. I.).

The basophilic degeneration index for the eight cases of atrophy of the thyroid gland was 40.5, and that for the eleven selected positive control cases was 7.7, showing a quantitative correlation between basophilic degeneration of the myocardium and atrophy of the thyroid gland.

AUTHORS.

Garvin, C. F.: Tricuspid Stenosis, Incidence and Diagnosis. Arch. Int. Med. **72:** 104, 1943.

Of 119 consecutive patients who died of rheumatic heart disease and were examined post mortem, 43 (36.1 per cent) showed involvement of the tricuspid valve; in 13 of these the process had advanced to definite tricuspid stenosis (10.9 per cent of the 119 cases).

No new symptoms or signs helpful in diagnosis were discovered. The study did emphasize, however, the importance of chronic organic rheumatic tricuspid insufficiency as an indication that stenosis is likely, for in each one of the seven cases of organic tricuspid insufficiency included in the series there was more or less stenosis.

Three cases of tricuspid stenosis were diagnosed clinically. One of the patients had very severe tricuspid stenosis, the circumference of the orifice measuring 3.5 cm. Nevertheless, clinically there was pulsation of the jugular veins and of the liver. Apparently, marked stenosis of the tricuspid valve need not prevent the phenomena of tricuspid insufficiency.

AUTHOR.

Weiss, S., Stead, E. A., Jr., Warren, J. V., and Bailey, O. T.: Scleroderma Heart Disease With a Consideration of Certain Other Visceral Manifestations. Arch. Int. Med. **71**: 749, 1943.

The clinical histories of nine patients with generalized scleroderma are reported. Post-mortem examinations were performed on two patients. These nine patients were selected for study because they all had symptoms and signs of heart disease. Both the clinical and the pathologic studies indicate that the sclerodermatous process is not confined to the skin but involves other organs. The cardaic failure is caused by myocardial scarring of an unusual type. Roentgen examinations may show involvement of the lungs. Dysphagia is common and esophageal stricture occurs.

These patients demonstrate that scleroderma heart disease is a clinical and pathologic entity.

AUTHORS.

La Due, John S.: Myxedema Heart: A Pathological and Therapeutic Study. Ann. Int. Med. **18**: 332, 1943.

Hydropic vacuolization, loss of striation, branching, pyknotic nuclei and irregularity in staining properties of the muscle fibrils are seen in myxedema heart but are not specific for this entity.

Thiamin and vitamin B complex are ineffective therapeutic agents for myxedema heart.

AUTHOR.

Selye, H., Hall, C. E., and Rowley, E. M.: Malignant Hypertension Produced by Treatment With Desoxycorticosterone Acetate and Sodium Chloride. Canad. M. A. J. **49**: 88, 1943.

The nephrosclerosis produced by desoxycorticosterone acetate overdosage in the rat is particularly pronounced if the animals are kept on a high sodium chloride intake. Under such conditions, desoxycorticosterone acetate causes a pronounced rise in systolic and diastolic blood pressure, marked diuresis with increased excretion of sodium and chloride, proteinuria and clinical signs of severe cardiac decompensation. In some instances death ensues, due to hemorrhagic lung edema.

The characteristic pathologic findings in rats so treated are hypertrophy and capsular fibrosis of the renal glomeruli with hyalinization of their ruft capillaries. Fibrosis, hyalinization, and even actual necrosis of the arteriolar walls is evident not only in the kidney itself, where the vasa afferentia are particularly affected, but also in the pancreas and the adrenal capsule. In the pancreas these vascular changes are frequently accompanied by edema and pronounced stroma proliferation. The experimental disease thus produced bears a striking resemblance to the hypertensive heart disease of renal origin as seen in man.

AUTHORS.

Grollman, A., Harrison, T. R., and Williams, J. R., Jr.: The Mechanism of Experimental Renal Hypertension in the Rat. The Relative Significance of Pressor and Anti-Pressor Factors. Am. J. Physiol. **139**: 293, 1943.

Unilateral nephrectomy or the application of cloth or collodion to one kidney caused hypertension in a small percentage of normal rats. The subsequent removal from such animals of the kidney, to which cloth or collodion had been applied, did not result in a significant decline of the elevated blood pressure. Total

nephrectomy in animals surviving sufficiently long tended to cause an elevation of blood pressure. The bearing of these experiments on the theories of the pathogenesis of experimental renal hypertension is discussed.

AUTHORS.

Katz, Y. J., and Goldblatt, H.: Studies on Experimental Hypertension. XXI. The Purification of Renin. J. Exper. Med. **78:** 67, 1943.

Extraction of finely ground fresh hog kidney with distilled water adjusted to pH 7.8 sodium hydroxide, followed by successive treatment, as described, with trichloracetic acid and acetone, gives renin in good yield of a purity suitable for physiologic studies and a good starting material for further purification. It contains 15 dog units per milligram of nitrogen.

Further successive purification of this material with ethyl alcohol and ammonium sulfate gives a preparation containing 130 dog units per milligram of nitrogen. The purest preparation hitherto reported contained 16.0 to 20.8 units per milligram of nitrogen. Preliminary Tiselius electrophoresis studies suggest homogeneity, but further studies to establish purity are in progress.

The properties of the most purified renin indicate that it is a protein. Its chemical and physiologic properties correspond to those of the material in crude renal extract which induces an elevation of blood pressure when it is injected intravenously.

AUTHORS.

Richardson, G. O.: Atherosclerosis of the Main Renal Arteries in Essential Hypertension. J. Path. & Bact. **55:** 33, 1943.

Of thirty-two cases of essential hypertension examined at autopsy, twenty-five showed the presence of atherosclerotic plaques in one or both main renal arteries, with varying grades of apparent stenosis.

Examination of 113 nonhypertensive controls showed plaques in eight cases. In only three of these were the lesions of comparable severity to those seen in the cases of essential hypertension.

These findings are discussed, and it is suggested that atheromatous plaques may be capable of producing renal ischemia and consequent hypertension analogous to experimental hypertension.

AUTHOR.

Page, I. H.: Hypotension and Loss of Pressor Response to Angiotonin as the Result of Trauma to the Central Nervous System and Severe Hemorrhage. J. Exper. Med. **78:** 41, 1943.

Angiotonin refractoriness and hypotension follow upon injury to the central nervous system in dogs and cats. Refractoriness does not develop when the nervous system is quickly and expertly destroyed or the activity of the nervous system depressed by widespread injection into it of a local anesthetic. The syndrome develops in the absence of the kidneys and the suprarenal glands.

Glycine, methyl isothiourea, and rest are the only agents studied which tends to restore responsiveness, and the first two of these have only an irregular and temporary effect.

There is a marked degree of specificity in the syndrome since undiminished pressor responses to adrenalin, tyramine, and methyl isothiourea are observed during complete angiotonin refractoriness.

Despite the prolonged hypotension, change in the amount of plasma proteins and in the hematocrit readings is not striking.

Parallelism seems to exist between the fall in blood pressure after trauma to the nervous system and development of angiotonin refractoriness. After the syndrome has developed, elevation of the blood pressure by the injections of gum acacia solution or whole blood does not restore the responsiveness to angiotonin.

Angiotonin refractoriness and hypotension also develop after marked hemorrhage. Suprarenalectomy or nephrectomy does not prevent its appearance.

AUTHOR.

Logue, R. B.: Dissecting Aneurysm of the Aorta. Am. J. M. Sc. 206: 54, 1943.

A study of dissecting aneurysm of the aorta is presented. An ante-mortem diagnosis was made in ten of the twelve cases observed and confirmed on necropsy.

Isolated instances of dissecting aneurysm complicating calcareous aortic stenosis and syphilitic aortic insufficiency are presented. A new sign of this disease is described, consisting of a bruit and thrill over the femoral artery.

A history of previous hypertension, or an elevation of the blood pressure at the time of admission, was noted in eleven of the twelve cases.

Tamponade was the cause of death in seven cases. Hemorrhage into the pleural cavity, uremia, coronary occlusion, and ventricular fibrillation were the other causes of death.

AUTHOR.

English, J. P., and Willius, F. A.: Hemorrhagic Lesions of the Coronary Arteries. Arch. Int. Med. 71: 594, 1943.

Hemorrhagic lesions were observed in the walls of the coronary arteries in 54 of 135 hearts (40 per cent) and were directly or indirectly related to acute occlusion of the coronary artery in 20. The lesions were characterized by hemorrhage associated with the presence of large lipoid-containing cells, proliferative intimal changes, and organization. Smaller, less active lesions usually were found adjacent to calcified plaques. The intimal changes that coexisted with the hemorrhage appeared to represent the primary factor in the pathologic condition; the hemorrhage was secondary. It does not seem logical, moreover, that hemorrhage in itself can have produced the effects observed.

AUTHORS.

Graef, I.: Medial Hypertrophy of the Renal Arterioles in Pregnancy. Am. J. Path. 19: 121, 1943.

A case is reported of chronic unilateral hematuria in a colored female, 29 years old, who was cured by nephrectomy during the fifth month of pregnancy. The removed kidney revealed unusual, massive, medial hyperplasia and hypertrophy of the arterioles. There was accompanying intimal fibromuscular hyperplasia of the interlobular branches of the renal artery. Focal fresh hemorrhagic erosions were found in the pelvis and ureter.

The medial hypertrophy could not be accounted for by any known or demonstrable injury. A hypothetical explanation is offered, based on the theory that hormonal activity during pregnancy might be responsible for changes in the arteriolar smooth muscle comparable to those found in the gravid uterus.

AUTHOR.

Holman, R. L.: Experimental Necrotizing Arteritis in Dogs. III. Bilateral Nephrectomy as Effective as Heavy Metal Injury in Its Production. Am. J. Path. **19:** 147, 1943.

Acute necrotizing arterial lesions affecting principally the large elastic arteries (aorta, endocardium of the left auricle, pulmonary and coronary arteries) have been produced with regularity in dogs by combining three factors: maintenance on a standard low-protein diet, plasma alteration (usually repeated daily injections of plasma obtained from healthy donor dogs), and heavy metal injury, both uranium nitrate and mercuric chloride.

In the present report it has been shown that bilateral nephrectomy can be substituted for heavy metal injury, thus indicating that renal injury rather than heavy metal as such is the essential factor.

AUTHOR.

Wikle, H. T., and Cabot, N.: Embolectomy for Riding Embolus of Abdominal Aorta. Surgery **13:** 264, 1943.

Although the patient died twenty-seven days postoperatively, from what was apparently pulmonary infarction, the authors feel that the case is of sufficient interest to be reported because it does prove again that patients with severe cardiac conditions can be subjected to major surgical procedures without immediate mortality.

Autopsy would have made the case complete, and it is to be regretted that such a report is not available. However, in summary, a case of riding embolus at the bifurcation of the aorta is reported; the patient withstood three major surgical procedures in spite of the fact that she had a severe cardiac condition; and technique of embolectomy has been illustrated.

AUTHORS.

Luke, J. C.: Retrograde Venography of the Deep Leg Veins. Canad. M. A. J. **49:** 86, 1943.

A technique for performing retrograde femoral venography is described, and, in the course of twenty-nine such venograms, it has been found that the valvular mechanism of the femoral vein and its deep tributaries will allow retrograde flow of a contrast medium down the vein, even in cases of a normal leg. This is in contradistinction to the saphenous veins where the normal valve stations resist high pressure when retrograde injection is attempted. It is pointed out that retrograde venography is of use when a clear filling of the femoral vein is desired, and has its main indication in determining the presence or absence of a previous "silent" femoral phlebitis.

AUTHOR.

Bellis, C. J.: Measurement of the Circulation Rate: A Review of the Methods. Surgery **13:** 27, 1943.

A brief historical review of the methods which have been used for the determination of the circulation rate has been presented. This information formed the basis for selecting sodium cyanide as the determinant in surgical patients. These results are described in a succeeding paper.

AUTHOR.

Bellis, C. J., Doss, A. K., and Craft, C. B.: The Circulation Rate After Operation, With Special Reference to the Effect of Position. Surgery 13: 35, 1943.

Usually, the cubital vein-to-carotid body time and ankle vein-to-carotid body time, as determined by the sodium cyanide method, is shortened after major surgery. In 191 cases, the average preoperative cubital vein-to-carotid and ankle vein-to-carotid body times were 17 and 36 seconds, respectively; postoperatively, the times were 14 and 32 seconds, respectively.

Circulation rates vary widely in patients with apparently normal circulatory systems.

Acceleration of blood flow postoperatively is probably related to the increased metabolic demands of the organism, which are manifest by increased temperature, pulse rate, and respiration.

Gravity retards the flow of blood from the upper and lower extremities, either when the position of the extremity itself is changed or when the longitudinal axis of the entire body is altered.

Fowler's position delays the return of blood from the lower extremities.

Ankle vein-to-carotid body circulation rate is shortened by active motion of the foot or toes and by elevation of the extremity.

AUTHORS.

Stewart, H. J., Carty, J. R., and Seal, J. R.: Contributions of Roentgenology to the Diagnosis of Chronic Constrictive Pericarditis. Am. J. Roentgenol. 49: 349, 1943.

Roentgenologic study is of considerable importance in the differential diagnosis of chronic constrictive pericarditis.

When venous engorgement, serous effusions, and hepatomegaly are present, indicating obstruction to the flow of blood through the heart, the composite roentgenologic picture pointing most conclusively to chronic constrictive pericarditis as a cause of this obstruction is as follows: A small or only slightly enlarged heart of abnormal configuration and often a rim of calcium at the periphery. The aortic knob is absent or flattened and deformed. Roentgenoscopic examination reveals the excursions of the margins to be diminished to the point that the heart seems almost to be standing still. When the patient is tilted from side to side, the heart remains fixed in the midline and fails to elongate when the diaphragms move downward. Pulmonary congestion is usually evident, pleural thickening or effusion and extrapericardial adhesions deforming or imparting abnormal motion to the diaphragm may be found. The kymogram confirms the marked decrease in the amplitude of pulsation over the borders of the heart and of the aorta.

Roentgenoscopic signs in the order of their diagnostic importance are: (a) limitation of the lateral shift of the anatomical axis of the heart with descent of the diaphragms when the heart is not greatly enlarged and there is no marked limitation of diaphragmatic motion; (c) decrease in the amplitude of cardiac pulsations over portions or all of the cardiac silhouette; and (d) paradoxic motion or deformity of the diaphragms due to the tugging of adhesions.

Calcification is the most reliable sign of chronic constrictive pericarditis, especially when the cardiac silhouette is enlarged, but is present in less than half of the cases and, when present, does not always indicate constriction of the heart. It is sometimes visible under the roentgenoscope but is best demonstrated in lateral roentgenograms, and, occasionally, heavy exposures are necessary to demonstrate its presence.

In the absence of calcification, the most common roentgenographic signs of chronic constrictive pericarditis are: (a) a small and flattened or absent aortic knob; (b) abnormal configuration of the cardiac silhouette, usually with a tri-

angular or globular shape and loss of the normal subdivisions of the borders; and (c) evidence of pulmonary congestion.

The size of the cardiac silhouette, when small, is of considerable importance, but a marked increase in size or evidence of cardiovascular disease of other etiology (hypertension and arteriosclerosis, for example) does not necessarily rule out the diagnosis of chronic constrictive pericarditis. In these cases the diagnosis is more difficult but can usually be made from the composite roentgenologic and clinical pictures.

There was no constant relationship between the thickness of the pericardium removed at operation and the size of the cardiac silhouette in roentgenograms.

The roentgen kymogram is of considerable aid in the diagnosis, especially in the study of the pulsations along the aorta and right border of the heart where the amplitude of pulsation was found to be most regularly reduced. In addition to the reduced amplitude of pulsation, flattening and irregularity of the diastolic peak of the wave is sometimes a helpful but less important finding. Pulsations of normal or greater than normal amplitude may be seen over portions or all of the left border.

No constant changes in the size or appearance of the cardiac silhouette or of the aorta were observed following operation. Some hearts became larger, others smaller. Increase in the amplitude of pulsations in the kymogram were regularly seen over portions or over all the cardiac silhouette but could not be related to the degree of relief afforded by pericardiectomy.

AUTHORS.

Sagall, E. L., Horn, C. D., and Riseman, J. E. F.: Studies on the Action of Quinidine in Man. I. Measurement of the Speed and Duration of the Effect Following Oral and Intramuscular Administration. Arch. Int. Med. 71: 460, 1943.

After the administration of a cinchona derivative to a human being, the electrocardiogram uniformly shows an increase in the time from the beginning of the Q to the end of the T wave. In the present study, this index of the effect of the human heart was used to measure the speed and duration of action of quinidine and quinine administered to human beings either orally or by intramuscular injection.

The effect became evident shortly after the administration of a single dose by mouth, reached a maximum in one and one-half to three hours, was then maintained at a slightly lower degree for three to five hours, after which it decreased, at first rapidly, then more slowly, and was no longer evident in twenty-four hours.

Quinine was much less effective than quinidine.

Larger doses of quinidine sulfate did not change the time of the maximum response, although the effect became evident sooner and was more prolonged.

The response to intramuscular administration of injectable quinidine (a solution of quinidine hydrochloride with urea and antipyrine) was much more prompt (within fifteen minutes) and the magnitude of effect was slightly greater, but the duration of effect was approximately the same as when an equivalent dose was given by mouth.

When doses are given repeatedly either orally or intramuscularly, the response at any moment is essentially the sum of the separate effects of the individual doses acting at that moment.

These results indicate that, in the treatment of acute arrhythmias, the administration of quinidine should be repeated at intervals of two to two and one-half hours. This permits observation of the maximum effect of the preceding dose before continuation of therapy with minimum loss of time.

If more rapid control of the rate is required, administration of the drug may be repeated at intervals of one hour until the desired degree of slowing is attained, after which, therapy can be continued at intervals of two to two and one-half hours.

In the treatment of acute arrhythmias, intramuscular administration should provide more constant and earlier response and eliminate the uncertainties and irregular absorption of oral medication. Intravenous administration is unnecessary and unwise.

AUTHORS.

Chavez, I.: Comparative Value of Digitalis and of Ouabain in the Treatment of Heart Failure. Arch. Int. Med. 72: 168, 1943.

In the face of the divergence of opinion about the value of ouabain in the treatment of heart failure, the comparative actions of digitalis and of ouabain are outlined and the results of twenty years' experience in the use of ouabain are set forth.

Digitalis and oubain have similar, but not identical, action on the decompensated heart. By way of comparison, digitalis exerts a more pronounced effect on the functions of sinus excitation and auriculoventricular conduction, which it depresses; ouabain, on the contrary, acts primarily on contractility and tonicity, which it stimulates.

Comparatively speaking, digitalis directs its chief effect on the differentiated, neuromuscular tissue of the heart; ouabain, on the undifferentiated, contractile fibers of the myocardium.

Digitalis, administered by the oral route, fixes itself slowly on the heart; ouabain, administered intravenously, acts with rapidity. The maximum effect of digitalis is reached in two or three days, whereas that of ouabain is reached in one or two hours. Digitalis accumulates; ouabain does not. On discontinuing the drug, digitalis extends its effects over a period of several days, up to eight or ten; those of ouabain disappear in twenty-four to thirty-six hours.

The best fields for the application of digitalis are: congestive heart failure with tachycardia and, especially, with auricular fibrillation; fibrillation even in the absence of heart failure; and long sustaining treatment of patients with slightly decompensated cardiac disease.

The best fields for the application of ouabain are the acute phenomena of failure of the left ventricle and chronic failure of the left side of patients with vascular disease, such as coronary arteriosclerosis, hypertension, and syphilitic aortitis.

The author recommends, as the best technique for the use of ouabain, one intravenous injection daily of 0.25 mg. in a series of six doses, and more, according to the tolerance of the individual patient and the clinical improvement obtained. In thousands of patients treated over a period of twenty years, the author has not encountered a single case of death attributable to ouabain.

AUTHOR.

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The Association earnestly solicits your support and suggestions for its work. Membership application blanks will be sent on request. Donations will be gratefully received and promptly acknowledged.

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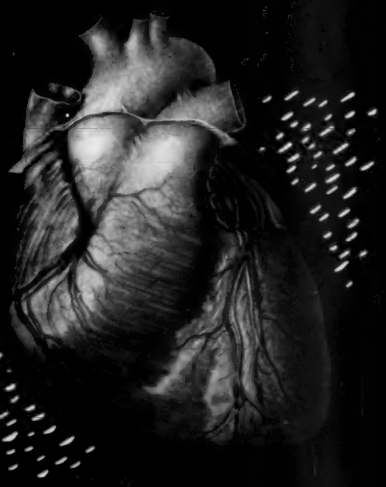

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